Food for the ageing population

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Introduction

The ageing population seen in many industrialized nations is a consequence of declining fertility and mortality in later life, this is often referred to as demographic ageing or population ageing (Gavrilov and Heuveline, 2003). Globally the proportion of older persons, defined as aged 60 years or over, has risen from 8% in 1950 to 11% in 2007, and is expected to reach 22% in 2050 (see Fig. I.1, United Nations, 2007). Currently over a fifth of the population in more developed countries is aged 60 years or over and this is projected to be over a third by 2050 (United Nations, 2007). The ageing trend can also be seen in the older population itself with the group 80 years or over increasing by 3.9% per year (United Nations, 2007).

Research has demonstrated that the elderly population is diverse in terms of its resources, needs, and abilities (Bengtson *et al.*, 1990). The older consumer market is agreed to be heterogeneous and attractive in terms of its size and the potential spending power (Long, 1998; Ahmad, 2002). Uncles and Ehrenberg (1990) highlighted the importance of recognizing this heterogeneity, distinguishing between the active older consumers whose requirements remain similar to those from when they were younger and the frail elderly or oldest old whose shopping and eating habits are constrained.

From a biological perspective the ageing process varies in terms of the way in which and speed with which it takes place and is based on the following principles:

1. *The evolutionary life history principle*, i.e. ageing is an emergent phenomenon seen primarily in protected environments which allow survival beyond the natural lifespan of a species, termed essential lifespan.
2. *The non-genetic principle*, i.e. although genes are involved in determining

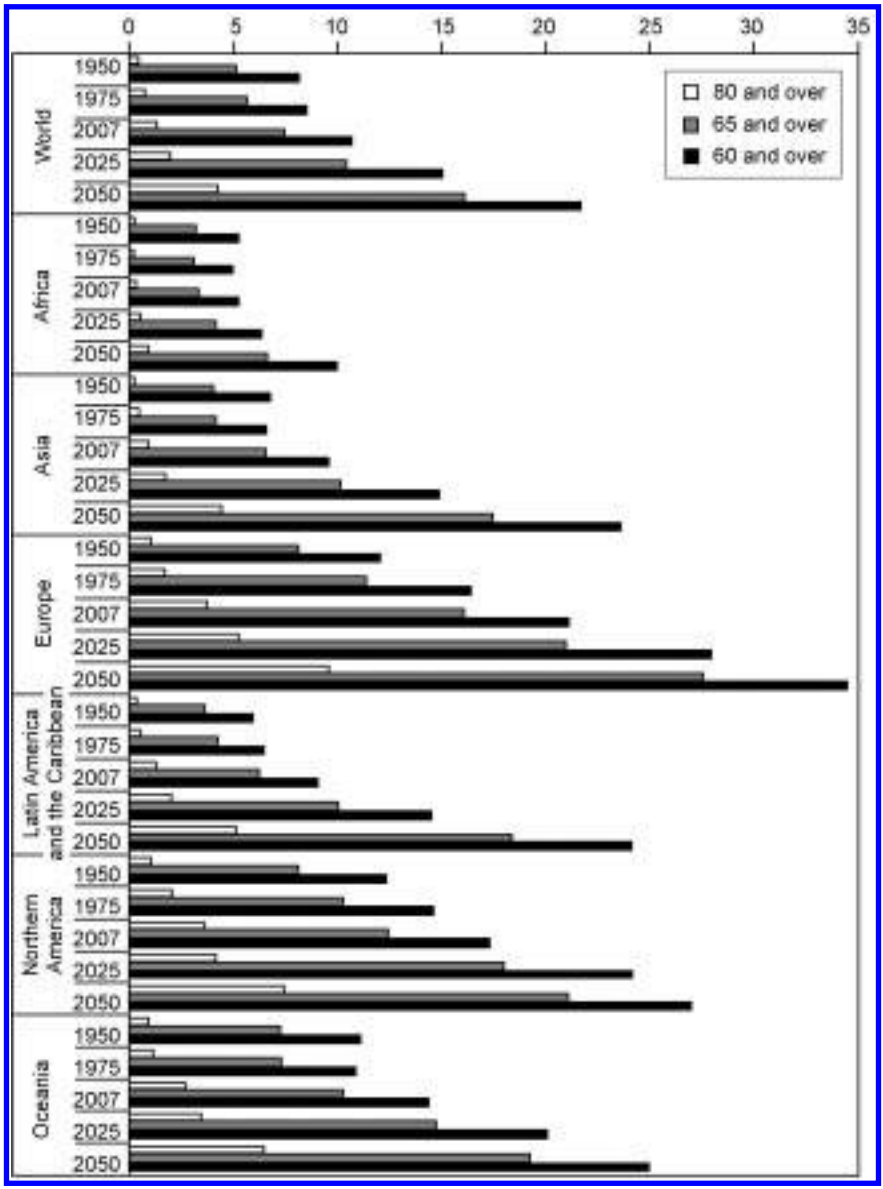

Fig. I.1 Percentage of population over 60, over 65 and over 80 in regions, estimates and projections (United Nations, 2007).

the essential lifespan of a species, ageing and longevity of an individual is not programmed in specific gerontogenes.

3. *The mechanistic principle*, i.e. accumulation of molecular damage and increased molecular heterogeneity is the cause of age-related failure of homeodynamics (Rattan, 2007).

A lifelong buildup of molecular damage leads to age-related frailty, disability and disease, and eventually to death (Kirkwood, 2008a). Frailty is characterized by diminished reserves in multiple organ systems resulting from disease, lack of activity, inadequate nutritional intake, stress, and/or the physiologic changes of ageing; and manifests itself as loss of skeletal muscle mass (sarcopenia), abnormal function in inflammatory and neuroendocrine systems, and poor energy regulation (Ahmed *et al.*, 2007).

The ageing process is very complex and influenced by factors intrinsic to the individual such as genes, and extrinsic factors that include environmental and lifestyle variables, such as nutrition and exercise; as well as chance or luck. It is estimated that only 25% of what determines length of life is accounted for by genes and the remaining 75% is accounted for by exogenous factors (Kirkwood, 2003). It is currently thought that the ageing process is much more malleable and could thus be delayed through preventing exposure to damage, for example by improved nutrition and other lifestyle habits, and by enhancing the body's natural mechanisms of protection and repair (Kirkwood, 2006). Stress, poor diet and an adverse environment can accelerate the rate with which damage occurs and the onset of age-related frailty and disease can be delayed as a result of good diet and other lifestyle factors (e.g. exercise) and a favourable environment (Kirkwood, 2008b).

Ageing is linked with deterioration in many of the body's physiologic functions, leading to structure changes, loss of lean mass and a relative increase in fat mass over time (Prinsley and Sandstead, 1990). The loss of appetite associated with ageing, sometimes termed the anorexia of ageing, is the physiological decrease in food intake occurring to counter balance reduced physical activity and a lower metabolic rate not compensated for in the long term (Morley and Silver, 1988). Ageing is also associated with a functional decline relating to taste and smell that can lead to decreased palatability of food and a potential failure to develop sensory specific satiety (Rolls, 1999). These changes can impact on the nutrient requirements of older people and for this reason tailored nutrient recommendations are being developed. Table I.1 provides an overview of micronutrients and their main functions. Table I.2 provides an overview of selected current micronutrient recommendations, focussing on recommendations that recognize older people as a specific group and have been established by bodies that have set their own recommendations as opposed to adopting those set by others.

An important distinction is that made by Rowe and Kahn (1987) recognizing successful, usual, and pathological ageing. Successful ageing is defined as decreasing the risk of diseases and disease-related disability whilst maintaining physical and mental functioning; and being actively engaged with life with 'active' referring not only to being physically or economically active, but also to continued societal participation (Rowe and Kahn, 1998). The World Health Organisation's active ageing policy framework (2002) identified and brought together the key concepts of 'productive ageing' (i.e. the ability to contribute directly and indirectly in older age, see Kerschner and Pegues (1998)) and

Table I.1 Micronutrients and their main functions (adapted from Porter *et al.*, 1995–2008)

Micronutrient	Main functions
Biotin	Required for the metabolism of carbohydrates and fatty acids
Folate (folic acid)	Required for the formation of red blood cells, for DNA and RNA synthesis, and for normal development of the nervous system in a fetus
Niacin (nicotinic acid or nicotinamide)	Required for the metabolism of carbohydrates, fats and many other substances
Pantothenic acid	Required for the metabolism of carbohydrates and fats
Riboflavin (vitamin B_2)	Required for the metabolism of carbohydrates and amino acids and for healthy mucous membranes, such as those lining the mouth
Thiamin (vitamin B_1)	Required for the metabolism of carbohydrates and for normal nerve and heart function
Vitamin A (retinol)	• Required to form light-sensitive nerve cells (photoreceptors) in the retina, helping maintain night vision • Helps maintain the health of the skin, cornea, and lining of the lungs, intestine, and urinary tract • Helps protect against infections
Vitamin B_6	Required for the metabolism of amino acids and fatty acids, for normal nerve function, for the formation of red blood cells and for healthy skin
Vitamin B_{12} (cobalamins)	Required for the formation and maturation of red blood cells, for nerve function and for DNA synthesis
Vitamin C (ascorbic acid)	• Required for the formation, growth, and repair of bone, skin and connective tissue, for healing of wounds and burns and for normal function of blood vessels • Acts as an antioxidant, protecting cells against damage by free radicals • Helps the body absorb iron
Vitamin D	• Promotes the absorption of calcium and phosphorus from the intestine • Required for bone formation, growth and repair • Strengthens the immune system and reduces the risk of autoimmune disorders
Vitamin E	Acts as an antioxidant, protecting cells against damage by free radicals
Vitamin K	• Helps in the formation of blood clotting factors and thus is necessary for normal blood clotting • Required for healthy bones and other tissues

Table I.1 Continued

Micronutrient	Main functions
Calcium	Required for the formation of bone and teeth, for blood clotting, for normal muscle function, for the normal functioning of many enzymes and for normal heart rhythm
Chloride	Involved in electrolyte balance
Chromium	• Enables insulin to function (insulin controls blood sugar levels) • Helps in the processing (metabolism) and storage of carbohydrates, protein and fat
Copper	Is a component of many enzymes that are necessary for energy production, for antioxidant action, and for formation of the hormone epinephrine, red blood cells, bone, and connective tissue
Fluoride	Required for the formation of bone and teeth
Iodine	Required for the formation of thyroid hormones
Iron	• Required for the formation of many enzymes in the body • Is an important component of muscle cells and of hemoglobin, which enables red blood cells to carry oxygen and deliver it to the body's tissues
Magnesium	Required for the formation of bone and teeth, for normal nerve and muscle function and for the activation of enzymes
Manganese	Required for the formation of bone and the formation and activation of certain enzymes
Molybdenum	• Required for metabolism of nitrogen, the activation of certain enzymes and normal cell function • Helps break down sulfites (present in foods naturally and added as preservatives)
Phosphorus	• Required for the formation of bone and teeth and for energy production • Used to form nucleic acids, including DNA (deoxyribonucleic acid)
Potassium	• Required for normal nerve and muscle function • Involved in electrolyte balance
Selenium	• Acts as an antioxidant with vitamin E • Required for thyroid gland function
Sodium	• Required for normal nerve and muscle function • Helps the body maintain a normal electrolyte and fluid balance
Zinc	• Used to form many enzymes and insulin • Required for healthy skin, healing of wounds and growth

Table I.2 Overview of selected micronutrient recommendations

	Food and Agriculture Organization of the United Nations, World Health Organization (2002)		Australia and New Zealand (National Health and Medical Research Council, 2005)		Netherlands (Food Nutrition Council, 1992; Health Council of the Netherlands, 2000, 2003)		United Kingdom (Panel of DRVS of the Committee on Medical Aspects of Food Policy, 1991)		DACH countries (German Nutrition Society, Austrian Nutrition Society, Swiss Society for Nutrition Research, Swiss Nutrition Association, 2000)		Nordic countries (Denmark, Finland, Iceland, Norway, Sweden) (Nordic Council of Ministers, 2004)		USA and Canada (Food and Nutrition Board, Institute of Medicine, National Academies, 1997, 1998, 2000, 2001, 2003)	
Type of recommendation	Recommended nutrient intakes		Recommended dietary intake		Recommended dietary allowance		Reference nutrient intake		Recommended nutrient intake		Recommended intake		Recommended dietary allowances	
Age range	>65 years		>70 years		≥65 years		>50 years		≥65 years		≥75 years		>70 years	
Gender	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Folate (folic acid)	400 μg		400 μg		300 μg (≥19 years)		200 μg		400 μg		300 μg		400 μg	
Niacin (nicotinic acid or nicotinamide)	16 mg	14 mg	16 mg	14 mg	17 mg (≥70 years)	13 mg (≥70 years)	16 mg	12 mg	13 mg		15 mg	13 mg	16 mg	14 mg
Riboflavin (vitamin B2)	1.3 mg	1.1 mg	1.6 mg	1.3 mg	1.5 mg (>70 years)	1.1 mg (>70 years)	1.3 mg	1.1 mg	1.2 mg		1.3 mg	1.2 mg	1.3 mg	1.1 mg
Thiamin	1.2 mg	1.1 mg	1.2 mg	1.1 mg	1.1 mg*** (>70 years)		0.9 mg	0.8 mg	1 mg		1.2 mg	1 mg	1.2 mg	1.1 mg
Vitamin A (retinol)	600 μg*		900 μg	700 μg	700 μg***	600 μg***	700 μg	600 μg	1000 μg	800 μg	900 μg	700 μg	900 μg	700 μg
Vitamin B6	1.7 mg	1.5 mg	1.7 mg	1.5 mg	1.8 mg (>50 years)	1.5 mg (>50 years)	1.4 mg	1.2 mg	1.4 mg	1.2 mg	1.6 mg	1.2 mg	1.7 mg	1.5 mg
Vitamin B12 (cobalamins)	2.4 μg		2.4 μg		2.8 μg (≥19 years)		1.5 μg		3 μg		2 μg		2.4 μg	

Vitamin C (ascorbic acid)	45 mg		45 mg		70 mg***		40 mg		100 mg		75 mg		90 mg		75 mg	
Vitamin D	15 μg		15 μg***	15 μg***	12.5 μg*** (>70 years)		10 μg		10 μg		10 μg		15 μg***			
Vitamin E	10 mg**	7.5 mg**	10 mg**	7 mg**	12 mg***	9.3 mg***	–	–	12 mg****	11 mg****	10 mg	8 mg	15 mg	15 mg		
Vitamin K	65 μg	55 μg	70 μg***	60 μg***	–	–	–	–	80 μg****	65 μg****	–	–	120 μg***	90 μg***		
Calcium	1300 mg		1300 mg		1200 mg*** (>70 years)		700 mg		1000 mg		800 mg		1200 mg***			
Iodine	150 μg	150 μg	150 μg		–	–	140 μg		180 μg		150 μg		150 μg			
Iron	9.1 mg[a] 11.4 mg[b] 13.7 mg[c] 27.4 mg[d]	7.5 mg[a] 9.4 mg[b] 11.3 mg[c] 22.6 mg[d]	8 mg		9 mg***	8 mg***	8.7 mg		10 mg		9 mg		8 mg			
Magnesium	224 mg	190 mg	420 mg	320 mg	325 mg	275 mg	300 mg	270 mg	350 mg	300 mg	350 mg	280 mg	420 mg	320 mg		
Selenium	33 μg	25 μg	70 μg	60 μg	100 μg***		75 μg	60 μg	30–70 μg****		50 μg	40 μg	55 μg			
Zinc	4.2 mg[e] 7 mg[f] 14 mg[g]	3 mg[e] 4.9 mg[f] 9.8 mg[g]	14 mg	8 mg	8.5 mg***	7.5 mg***	9.5 mg	7 mg	10 mg	7 mg	9 mg	7 mg	11 mg	8 mg		

[a] 15% bioavailability; [b] 12% bioavailability; [c] 10% bioavailability; [d] 5% bioavailability; [e] high bioavailability; [f] moderate bioavailability; [g] low bioavailability; * Recommended safe intake; **Acceptable intake; **Best estimate of requirements; ***Adequate intake; ****Estimated values for adequate intake

'healthy ageing' (i.e. the ability to remain physically and mentally fit). Healthy ageing is thus the ideal situation in which disability and morbidity are compressed into a relatively short period before death, preceded by a long period in which people age with their vigour and functional independence intact (Campion, 1998). 'Positive ageing' is a concept that has been used to characterize quality of life in old age (Bowling, 1993; Kendig and Browning, 1997).

The importance of diet in relation to ageing well has long been recognized but warrants further attention. This book explores the role that food and nutrition play in older people's lives, mainly those living in industrialized countries. The book was written with a broad audience in mind, including academics, practitioners (policymakers, those working in care and in food industry) with an interest in research issues related to food and the health of older people. In nutrition, primary prevention of disease relates to enhancing and maintaining wellness through food, whereas the focus of secondary prevention is that of maintaining or improving nutritional status and avoiding disease. This book is about prevention of, rather than the treatment of, disease and age-related pathologies.

In order to understand the potential impact food has on older people's health and quality of life, knowledge is needed of both consumer and underlying physiology. Once this is understood, optimal recommendations, products and services can be developed. The book consists of 28 chapters, each written such that it is 'readable as a whole'; thus there is to a limited extent overlap between chapters. Some chapters are very specific, others more general. The first part of the book 'Understanding older people as consumers of food and beverages' focuses on the role that food plays with regard to quality of life. The social and cultural aspects of food choices and meal patterns are addressed as well as sensory perception of food and satisfaction with food-related life. The second part of the book 'Extending functionality into later life' explores the importance of nutrition for health, its role in repair mechanisms and preventing exposure to damage. It focuses on the prevention of disabilities and diseases such as those associated with the metabolic syndrome and Alzheimer's disease. The final part of the book 'Developing food products and services for older people' covers topics such as food safety and preparation in later life, developing nutrition education interventions and designing new foods and beverages for the ageing population.

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Part I

Understanding older people as consumers of food and beverages

1

Older people, food and satisfaction with life

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Abstract: This chapter discusses food-related satisfaction with life of older people, identifying some of the determinants and barriers to satisfaction with food-related quality of life, and discusses possible ways of enhancing older people's quality of life in the domain of food. Despite being strongly associated with life, and heavily contributing to the quality of life, food has so far been neglected and not much research has been conducted into people's satisfaction with their food-related life and its relationship to overall life satisfaction. As people age, their goals and available resources in terms of health, social networks, income and skills change. Changes in resources can be expected to have an impact on satisfaction with life.

Key words: satisfaction, quality of life, older people, goals, resources.

1.1 Introduction

Dietary intake and nutritional status not only play a major role in the overall quality of health of older people but also have impact on their satisfaction with life (Sahyoun, 1999; Vailas *et al.*, 1998). Silverman *et al.* (2002) argue that the type of food eaten and the social cultural context all make significant contributions to older people's satisfaction with their quality of life.

Investigating satisfaction with food-related life of older people has high significance for several reasons. Firstly, food and energy intake tend to decrease with ageing for a number of both physiological and practical reasons including reduced activity (immobility), reduced muscle tissue, a lower resting metabolic

rate and smaller meals (Macintosch *et al.*, 2000; Prinsley and Sandstead, 1990). This reduced energy intake, also known as 'anorexia of ageing', is a potential health risk because, although food intake is reduced with age, the need for most nutrients does not decrease with age. Secondly, ageing affects the ability to taste and smell. Also seniors are less sensitive to all the basic tastes and particularly smells. Both the ability to detect tastes and smells and their intensity decline with age and it has been suggested (Rolls, 1999; Westenhoefer, 2005) that sensory losses accompanying ageing may even be partly responsible for the reduced intake of foods (see Chapter 4). Further as people get older their living circumstances may alter. For example, as people retire, their level of income may reduce and their social network may also diminish. As health fails, access to shops and amenities may become a problem. As people lose their living companions due to death of spouse, or children leaving home, cooking arrangements may change. All these factors compound as people get older, affecting older people's relationship with food and in turn their satisfaction with food-related life. By identifying which factors are important and what can be altered, it may be possible to increase older people's satisfaction with food and in turn contribute to a better quality of life. This chapter looks at food-related satisfaction with life of older people, identifying some of the determinants and barriers to satisfaction with food-related quality of life, and discusses possible ways of enhancing older people's quality of life in the domain of food.

1.2 Satisfaction and quality of life

Concepts such as quality of life, subjective well-being and life satisfaction are generally used in relation to older people when investigating the impact of ageing (Lumbers and Raats, 2006). As society changes, people's experience of ageing and later life also alters (Wiggins *et al.*, 2004). As health care and consequently life expectancy has increased (Office of National Statistics, 1998; Blaikie, 1999) and retirement age decreased (Gruber and Wise, 1999), these changes have had great impact on older people's satisfaction with their quality of life. Gabriel and Bowling (2004) argue that research in the US investigates variables that contribute to the 'good life' and address both the positive and negative aspect of ageing. In Europe, on the other hand, they claim that the emphasis is on the functional aspects of ageing, which tend to be negative and more concerned with dependency, poverty, service needs and decline in mental and physical health, although they acknowledge that there is a gradual shift from this perspective towards one where old age is seen as one providing personal fulfilment.

Wiggins *et al.* (2004) claim that older people's quality of life is shaped by age, gender, accommodation and environment of past life, pension provision, health status, current housing and whether or not they have access to a car. However, despite being used frequently in the literature, quality of life is not a clearly defined construct and is usually used to describe different physical and psychological factors (Moons *et al.*, 2006). There is no consensus about how it is

defined or how it should be measured (Felce, 1997; Haas, 1999; Moons *et al.*, 2006; Zhan, 1992). The measurement of the quality of life construct usually includes both objective measures and subjective perceptions (Moons *et al.*, 2006), where the subjective part is often referred to as 'subjective well-being', and divided into affective and cognitive parts (Andrews and Withey, 1976). The cognitive component is a subjective, judgmental evaluation of life circumstances which is a global assessment of a person's quality of life according to his/her chosen criteria. The most well-known measure of subjective well-being is the Satisfaction With Life Scale developed by Diener and his colleagues (Diener *et al.*, 1985). If the factors influencing one's satisfaction with quality of life are known, it is possible to intervene and find ways of improving satisfaction with life.

Researchers have partitioned life into multiple domains and view satisfaction with quality of life as a composite measure of satisfaction in each of these domains (Andrews and Withey, 1976; Campbell *et al.*, 1976; Day, 1987; Diener, 1984; Hsieh, 2003). Here a domain is viewed as an aspect of life about which people have feelings (Andrews and Withey, 1976) or as an area of human experience that most people find significant (Campbell *et al.*, 1976). Domain-specific satisfactions with life measures are useful when assessing the effect of changes in life circumstances in a specific domain. Headey *et al.* (1991) divide life into six domains: marriage, work, material standard of living, leisure, friendship and health, whereas Hsieh (2003) divides life into eight domains: health, work, spare time, financial situation, neighbourhood, family life, friendships and religion. Argyle (2001), on the other hand, divided life into domains such as money, health, work and employment, social relationships, leisure, housing and education. Whilst the domains proposed have been arbitrary, diverse and to some degree overlapping (Cummings, 1996), one very important life domain, food, has consistently been neglected in the various instruments presented in the literature.

1.3 How does food contribute to quality of life?

Food is so important that it permeates all aspects of human life and engages and interjects with almost all of our activities: leisure, arts, sex and work. Despite being strongly associated with life, and heavily contributing to the quality of life, food has so far been neglected and not much research has been conducted into people's satisfaction with their food-related life and its relationship to overall life satisfaction.

In the health domain, a broad quality of life measure has been used in nutritional studies (Schlettwein-Gsell, 1992; Barr and Schumacher, 2003; Jackson *et al.*, 2005), to measure baseline status and intervention effects. Dietary intervention studies measure outcomes from a patient perspective, most notably in the clinical areas of diabetes, cardiovascular disease, renal disease and enteral feeding (Jackson *et al.*, 2005). Recent attempts to construct a quality of life

instrument for specific use in nutrition studies have contributed to the construction of the Nutrition Quality of Life Survey (Barr *et al.*, 2001; Barr and Schumacher, 2003) and the Quality of Life Factors Questionnaire (Corle *et al.*, 2001). Both instruments are broad, multi-dimensional measures, combining general and domain-specific components, as well as combining self-reported objective indicators and subjective evaluations of well-being. Whilst the Quality of Life factors questionnaire includes four items on life satisfaction, neither instrument includes a measure of satisfaction with food-related life.

Grunert *et al.* (2007) have devised a measure of Satisfaction with Food Related Life that is loosely based on the Quality of Life factors questionnaire, but with a focus on food-related behaviours. The investigators validated the measure on older people in eight European countries. The instrument consists of five items to be answered on a 7-point scale. Figure 1.1 shows mean satisfaction with food-related life in the eight-country study, and also shows, for each country, the correlation between satisfaction with food-related life and overall life satisfaction. Satisfaction with food-related life was highest in Germany and the UK, and lowest in Poland, Italy and Portugal.

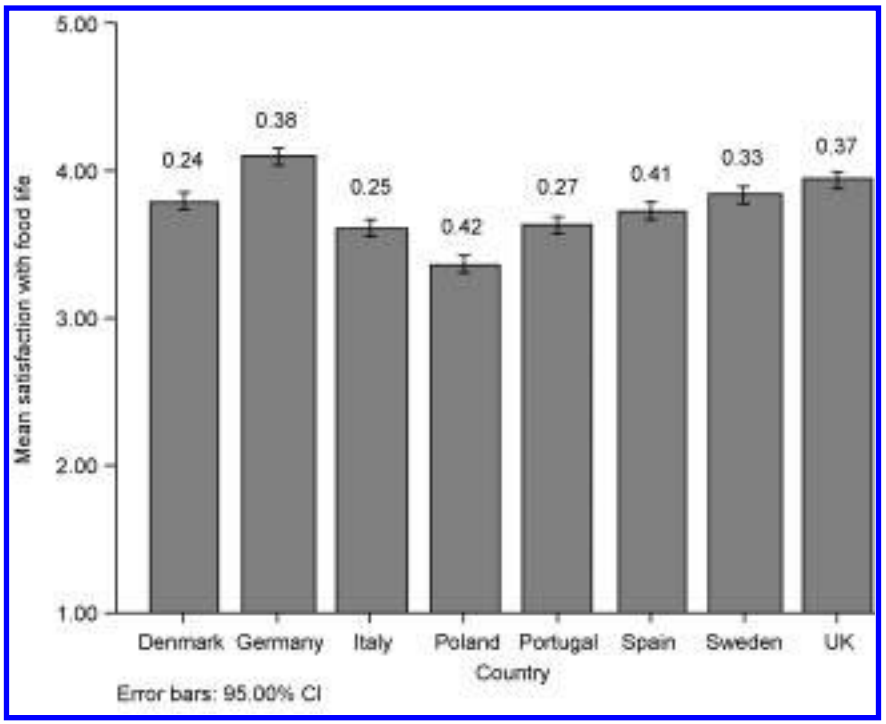

Fig. 1.1 Mean satisfaction with food-related life and correlation with overall life satisfaction (Scale 1–5; 1 – low importance, 5 – high importance). Total of 3291 respondents in Denmark, Germany Italy, Poland, Portugal, Spain, Sweden, UK, quotas for age (65–75/older), gender and living alone/with partner.

1.4 Factors impacting on satisfaction with food-related life

Research suggests that demographic factors such as gender, age and living arrangements, social factors such as number of friends, closeness with friends and/or closeness with family, economic factors such as level of income and access to transport affect people's diet, health and ultimately satisfaction with their quality of life (Wiggins *et al.*, 2004). As people get older, many of these factors change and affect older people's relationship with food and food-related satisfaction with life.

Lower levels of economic resources are associated with greater risk of experiencing hunger and food insufficiency (Brown, 1987; Sahyoun and Basiotis, 2001). Low economic resources can also affect the quality and quantity of food purchased (Quinn *et al.*, 1997). Some research has suggested that it costs more to eat a more healthy diet (Blaylock *et al.*, 1999). Thus, low income restricts not only the quantity but also the nutritional quality of food purchased. Low income also reduces consumers' ability to substitute market produced meals for home-cooked versions as their desire and ability to shop and prepare meals declines (Sharpe *et al.*, 2003).

Research indicates that health problems related to inadequate nutrition are more prevalent in rural areas (Quandt and Chao, 2000; Schoenberg, 2000; Shotland and Loonin, 1988). Rural residents also mention transport to and from food markets as a structural barrier to obtaining adequate food (Hendy *et al.*, 1998; Lee *et al.*, 1998; Wallace *et al.*, 1997). Sharpe *et al.* (2003) found that rural and low income single elderly women were significantly less likely to eat a nutritionally adequate diet than were their non-rural and higher income counterparts. Lack of nearby supermarkets with adequate selection of healthy foods or access to support programmes such as Meals-on-Wheels may also serve as important constraints to healthy eating for the rural elderly.

Quandt and Chao (2000) note that women, more so than men, report chronic problems with oral health and digestion, need for special diets, disease interference with eating and anaemia. Gender differences in nutritional behaviour have been noted in many different cultures (Silverman *et al.*, 2002). In many of the US studies there has been a marked difference between men and women in their nutritional behaviour. Hendricks *et al.* (1988) found that gender not only influences what one eats, but also the social patterns that can influence food-related practices. Studies have shown that for several decades food-related activities were the prime responsibility of the women in the role of wife and mother (Murcott, 1982; 1983; Charles and Kerr, 1988). Women not only performed this duty uncritically, but also prepared food that was to the taste of their husband rather than their own. Even when husbands and wives were both in full employment and sharing food preparation, the main responsibility for food supply was found to be on the women's shoulders. However, in these circumstances, the wives were not pandering to the husbands' tastes as they did when they were the sole cooks (Kemmer, 1999). Recent studies (Lake *et al.*, 2006) showed that food shopping and preparation were still heavily gendered, where

men were viewed (by themselves and by the women) as impulsive shoppers, only getting involved in cooking on special occasions rather than sharing daily cooking activities (see Chapter 6 for detailed analyses on differences between the genders in food preparation).

Mason (1987) found that when these men retired and both partners were, for the first time, in a position to share domestic responsibilities, taken-for-granted gender segregated roles still remained. In 1997 Sullivan observed that negotiations had occurred within these roles so that the men performed some cooking and housework, while the women retained the 'management' role. Research suggests that after retirement, women still do most of the work in the domestic sphere, and only relinquish their responsibilities (but sometimes retaining the management role) when they are too ill to do them. Davidson, Arber and Marshall's results (see Chapter 6) suggest that for many of the married older women there was still a connection between enjoyment of food preparation and preparing foods for others, specifically their husbands. Thus it is reasonable to expect differences between older men's and women's satisfaction with food-related quality of life. Whether or not women are more or less satisfied may depend on whether they saw their involvement with food as part of their goal in life.

Many researchers argue that eating is not only about nutritional intake, but also a social occasion such that people don't consider a meal to be 'proper' or 'ideal' when eaten alone (Sobal, 2000; Douglas, 1972; Murcott, 1982). There is evidence that living alone is associated with various health-related disadvantages. Murphy (1997) reported that in Britain rates of long-standing illness in middle age were higher among those who lived alone compared with those in other types of household. However structural and demographic changes in society have increased the probability of eating alone. Older people's eating arrangements appear to be changing with elderly people increasingly less likely to live with family members or unrelated members and more likely to live alone (Sundstrom, 1994; Kinsella and Velkoff, 2001). The type of living arrangement can have a profound effect on whether or not one is able to share meals with others.

Social isolation often exacerbated by deterioration of sight, hearing and mobility, leaves many elderly living and eating alone. Physical disabilities, such as difficulty in walking, grocery shopping, and preparing food, further restricts the amount and types of foods available. Similarly, missing, decaying or loose teeth or ill fitting dentures make it hard for older people to eat an appropriate variety and quantity of foods, as do difficulties with chewing, swallowing and digestion. In addition, altered mental states such as confusion and memory loss affect a large segment of the older population, making it hard to remember what, when and if one has eaten, limiting the ability to eat an adequate diet or enjoy it.

Studies on older people's eating arrangements showed that whilst eating programmes such as attending a day centre (Smith *et al.*, 1994) and Meals-on-Wheels (Keller, 2006) may provide nutritious meals, they did not result in any enjoyment or contribute to their quality of life. This was found to be especially true for those who had lost their spouse, for women in particular (Shahar *et al.*, 2001; Sidenvall *et al.*, 2000; Wylie *et al.*, 1999; Quandt *et al.*, 1997).

Hetherington *et al.* (2006) in a UK-based study found that sharing a meal with family, or familiar others, increased energy intake by 18 percent compared to eating alone, followed by watching TV whilst eating alone, although eating together with strangers did not result in an increase in food intake. Thus changes in food-related routines, meals and social relations in everyday life can be expected to have long-term negative effects, if not on older people's nutritional status, at least on their feeling of well-being and quality of life. However, most of these studies were carried out on older women living alone. A study by Hughes *et al.* (2004) on older men found that most of the men in the study believed they had adequate cooking skills and their life satisfaction was good despite their vegetable and fruit intake not meeting the required nutritional level. Compared to older women, older men seem to have a more positive relationship to food, which may explain their contentment with food in everyday life. This suggests that there may be gender differences in how living arrangements affect older people's satisfaction with food-related quality of life.

A recent EU study (Raats and Lumbers, 2007) that investigated older people's satisfaction with food-related life in eight European countries found that on the whole men were more satisfied with their food-related life than women, and participants who lived with a partner were more satisfied than those who live alone. In addition the results showed that whilst living alone both men and women were equally satisfied with their food-related life, when living with a partner, men were significantly more satisfied than women (see Fig. 1.2).

Loneliness due to death of a spouse or friends can diminish the social reasons for and pleasures associated with eating (Shifflett and McIntosh, 1983; Walker and Beauchene, 1991). Eating regular meals and having an adequate diet have been found to depend, at least in part, on eating with others (Doan, 1990; Shifflett and McIntosh, 1983). Fewer than a third of a nationally representative sample of elders experiencing food insufficiency were married, compared with more than half of those consuming an adequate diet (Sahyoun and Basiotis, 2001).

Murphy *et al.* (1990); Walker and Beauchene, (1991) argue that loneliness rather than living alone may be the real cause of reduced food intake. Thus problems with loneliness, besides being deprived of human contact, may have an effect on nutritional status as well as people's satisfaction with food-related quality of life. A study by Walker and Beauchene (1991) showed that, among older persons age 60–94 years, loneliness and social isolation were related to dietary inadequacies. Although never-married older people have been found to be more isolated than married individuals, they are similar to them with respect to loneliness and life satisfaction (Gubrium, 1974). Dissatisfaction with available relationships may be a more powerful indicator of loneliness than the number of social contacts (Revenson and Johnson, 1984). The number of social contacts *per se* had no relationship with food choice and dietary adequacy (Walker and Beauchene, 1991). Social interactions at mealtimes in different settings were shown to improve dietary adequacy including those living independently and those in sheltered housing. This suggests that older people who live with a spouse are not necessarily less lonely and that care needs to be taken when people's

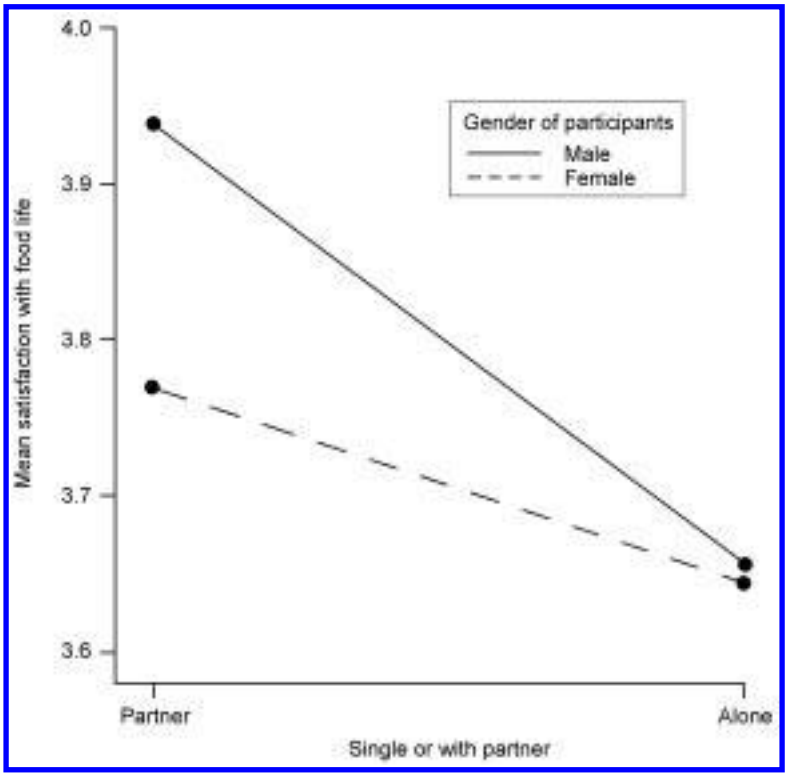

Fig. 1.2 Interaction of living arrangements and gender on satisfaction with food-related life (Scale 1–5; 1 – low importance, 5 – high importance). Total of 3291 respondents in Denmark, Germany Italy, Poland, Portugal, Spain, Sweden, UK, quotas for age (65–75/older), gender and living alone/with partner.

satisfaction with food-related quality of life is investigated such that the effects of gender, involvement, living arrangements and level of loneliness need to be looked at separately and jointly so as to get a clearer picture of the mechanisms and how people's satisfaction level could be improved.

Loss of a spouse (widowhood) is regarded as one of the most traumatic experiences in life (Lopata, 1996). In addition to the grief felt for the lost partner, the individual must adjust to a variety of new roles and tasks that may have previously been performed by their spouse. For older generations, where the division of labour around food-related tasks is usually highly gendered, widowers may face the task of food preparation for the first time in their lives (Bennett *et al.*, 2003). Similarly widows may be thrust into the alien experience of cooking for one and their own food preferences (Sidenvall *et al.*, 2000). Freedom from domestic duties may be valued by widowed women, but most widowers may be burdened when they have to fulfil domestic duties formerly carried out by their wives (Davidson, 2001). The shift from spouse to widow(er) is thus intimately tied up with changes in domestic roles associated with food preparation and eating meals.

This suggests that widowhood is a particularly vulnerable and volatile period where the quality and variety of older people's diet may suffer, affecting their energy intake and nutritional balance. The shift in domestic responsibilities together with the loneliness and isolation that follow may have a great impact on older people's satisfaction with food-related quality of life and on their overall quality of life. However, there may be gender differences on satisfaction with food-related quality of life depending on how widows interpret their situation. If, in such circumstances, widows start to enjoy the freedom to prepare and eat what they like and are not constrained by their spouse's preferences, then although they may be unhappy with their overall quality of life, they may become more satisfied with their quality of life in the food domain. On the contrary, widowers who have had their meals prepared and cooked for them all their married life may feel much less satisfied when they have to prepare and cook their own meals and thus eat a much narrower diet due to lack of skill or motivation.

In terms of social networks, some studies (e.g., McIntosh *et al.*, 1989; Davis *et al.*, 1990; Prothro and Rosenbloom, 1999) have found that strong social networks have a positive effect on diet, whereas other studies (e.g., Rothenberg *et al.*, 1993) show that diet is not affected by a poor social network. Sahyoun and Zhang (2005) showed that people with fewer social contacts had significantly lower healthy eating scores, consumed fewer calories, ate less varied diets and consumed fewer portions of fruit and vegetables. This suggests that those with a good social circle had a better diet and so you would expect them to be more satisfied with their food-related quality of life.

Caraher *et al.* (1999) investigated whether differences in cooking skills might be a factor in health differences and found there were differences between the sexes, age groups, income and social class with the greatest variation observed in gender. Learning cooking skills was determined primarily along the gender lines but also by social class and income. Older men may particularly lack motivation, knowledge and skills for meal preparation, resulting in less healthy food choices and narrow diets (Caraher *et al.*, 1999). This illustrates how the resources people have interact with demographic factors to influence people's diet. Having the skills needed to prepare and cook food may make people feel competent, thereby boosting their self-esteem which in turn will add to their satisfaction with food-related quality of life. Thus it could be argued that involvement with food preparation and cooking is one way by which older people can increase their satisfaction with food-related quality of life.

1.5 Food-related goals and resources

Researchers on subjective well-being and life satisfaction see products and services as important resources that play a major part in determining individuals' overall satisfaction with life, as these are viewed as helping people fulfil their needs (Cambell *et al.*, 1976, Heller *et al.*, 2004; Hobfoll, 2001). An individual's resources can be seen as means that are at the individual's disposal which he/she

can use to work towards achieving the most important goals to make him/her satisfied with his/her life. As people get older their goals change, and their available resources in terms of health, social networks, income and skills also change. Thus changes in resources would be expected to have an impact on older people's satisfaction with life.

Studies have shown (Diener and Diener, 1993; Veehoven, 1991) that the above-mentioned resources vary in relevance to subjective well-being depending on the values, needs and goals of the people involved. For a person to fulfil one or more goals and be satisfied with life, many different resources may be necessary. Even when different individuals pursue the same goal they may regard different resources as most instrumental to attain that particular goal. Diener and Fujita (1995) found that people tend to have goals that are relevant to their strongest resources. Also people who have the most congruent goals and resources – those who rated as being strong in the resources they perceive as most relevant to their goals – show the highest subjective well-being. They argue that successful adaptation is likely to depend on choosing goals that can be accomplished with the resources one possesses. Alternatively, people with high subjective well-being are better able to cultivate the resources they need to obtain their goals. For older people, when certain resources are diminishing it could be argued that those with goal-relevant resources would have a higher level of satisfaction with life than those whose resources are not congruent with their goals or lack the resources to achieve their goals. For example, as people get older, their health and income (resources) may diminish. At such a time, those individuals whose food-related goal is 'enjoying eating in the company of others' will still have a high food-related quality of life as long as they have the congruent resources such as a large network of family and friends helping to achieve their goal. However, others with goals such as 'choosing foods that they enjoy' and 'eating a wide choice of foods' may not be able to maintain their food-related quality of life with these similar resources due to the lack of congruence between their goals and the resources they possess.

Concepts similar to those suggested by Diener and Fujita (1995) may be applied to study satisfaction with food-related life to see how food-related goals and resources of older people may help us understand ways of enhancing older people's satisfaction with food-related life. By identifying older people's food-related goals and the relevant resources they possess, ways of improving the resources they need to fulfil their goals may be targeted. This may help to increase many older people's satisfaction with food-related quality of life.

Sirgy (2006) hypothesized that goals not only contribute to individuals' well-being through goal attainment but also through the feelings of hope and anticipation directly attributable to the goals. Cantor and Sanderson (1999) specified three dimensions of resources:

1. personal resources such as health, traits, strategies and abilities;
2. social resources such as social networks and social support;
3. material resources such as money, power and status.

They theorized that subjective well-being is not only dependent on goal attainment but also on the extent to which the goals are congruent or incongruent with one's own personal resources. Those with resources that match their goals are more likely to attain these goals than those whose goals do not match their resources. Thus older people who change their goals to be in line with resources they already possess will increase their satisfaction with food-related quality of life.

Kasser and Ryan (1996) distinguished between intrinsic and extrinsic goals. Examples of intrinsic goals include having good social relationships with loved ones, making significant contribution to the community, helping others in need, personal growth, maintaining good health, among others. Extrinsic goals include desire to make more money, desire to control people, attain social recognition, etc. It could be argued that 'food-related goals' aligns itself more to intrinsic goals as it is linked more with health and social relationships than with money and recognition. According to Kasser and Ryan, intrinsic goals tend to contribute to subjective well-being more so than extrinsic ones. Murray and Peacock (1996) found that number of friends, closeness of friends, closeness of family and relationships with coworkers and neighbours accounted for 70% of the variance in personal happiness. When people retire they lose many of their extrinsic goals and so intrinsic goals may take on a higher significance. Thus it can be argued that by helping older people to focus on these goals, identifying relevant resources, aiding them to get these resources and helping them achieve their goals may help to enhance their satisfaction including satisfaction with their food-related quality of life.

In a major European study on food in later life (Raats and Lumbers, 2007), a range of qualitative studies resulted in a list of resources of potential relevance for older people's satisfaction with food-related life. Figure 1.3 shows this list and the mean relevance of each of the resources for achieving the goals one has for food-related life, as perceived by respondents in a survey of older people in eight European countries. Adequate food storage facilities, ability to taste and smell, dental and general health as well as family support are regarded as important resources, whereas access to food service, and to organic, new or convenient products was regarded as less relevant.

1.6 Ways of enhancing quality of life through food

Studies have shown that gender impacts on the experience of food-related quality of life, with men being more satisfied than women. Further, men living with a partner were more satisfied than women in similar condition. Women on the whole were found to be still preparing most of the food, trying to please their partner's taste and preferences. Further, women live longer, thus having a greater chance of living alone for longer than men and on average having less money. All these may contribute to why women's level of satisfaction is lower than that of men. Thus to enhance women's satisfaction with food-related life

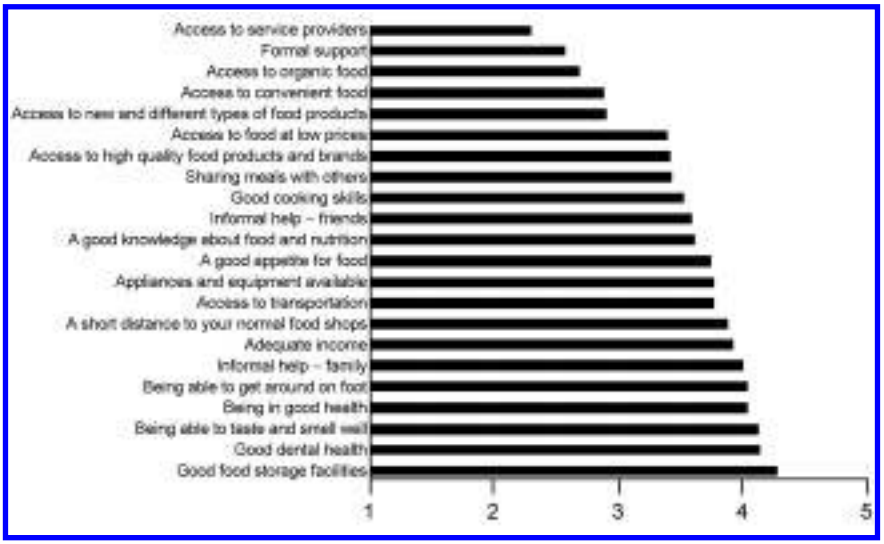

Fig. 1.3 Mean relevance of resources for achieving personal goals with food-related life (Scale 1–5; 1 – low importance, 5 – high importance). Total of 3291 respondents in Denmark, Germany Italy, Poland, Portugal, Spain, Sweden, UK, quotas for age (65–75/older), gender and living alone/with partner.

one would need to address their food-related goals and the congruent resources they possess. One means of achieving this would be to encourage women to re-evaluate their goals and to get them identify food-related goals that are important to them. Then by assessing the resources they have and by looking at the goal–resource fit different strategies could be planned to enrich this and thereby increase women's satisfaction with food-related life.

Social setting was found to be a determinant of satisfaction as well as nutritional behaviour. Older people eating in the company of friends and family had a better quality diet and were happier. Different ways of increasing communal eating in both private (e.g., own home or that of family or friends) and public (e.g., cafes, restaurants, luncheon clubs) settings where older people can socialize and eat together in a nice environment would enhance older people's food-related satisfaction.

Widowhood was shown to affect males and females differently in relation to their satisfaction with food-related life thus suggesting there is a need for different strategies for men and women. For widowers who have to start cooking for the first time or have had limited experience in the kitchen, cooking classes to address the lack of skill, nutritional information to address lack of information and re-evaluation of food-related goals to address lack of motivation will all contribute to enhancing their satisfaction with food-related life. For widows re-evaluating their goals in terms of prioritizing cooking for their own tastes and preferences rather than those of their partner, readjusting to cooking for one and evaluating their resources in terms of money and transport may help to enhance their food-related satisfaction.

Finally, involvement with food is shown to add to satisfaction. Finding ways of encouraging older people, both men and women, to incorporate food-related goals in terms of procurement, preparation or consumption into their daily life and finding resources that will help them realize these goals may help to increase older people's satisfaction with food-related life.

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2

Demographic and cultural differences in older people's food choices and meal patterns

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Abstract: Food choice affects healthy ageing and ageing affects food choice. The antecedents of food choice may be remote and even intergenerational. Culture and ethnicity are enduring influences on food choice whether from within one's group or through the pressures of conformity to a majority in a minority culture. This is particularly relevant to indigenous and migrant peoples and where older people are marginalized or isolated for economic, health or societal reasons. Different food cultures, from China, Japan and Korea in North East Asia to Sub-Saharan Africa, to Southern and Northern Europe, to Australasia may allow similar health outcomes. But food patterns for the aged are optimal where there is variety, especially of plant-derived food, regular consumption of legumes (pulses) and even small quantities of animal-derived food such as eggs, dairy, lean meats and fish, especially where energy through-put is low. The interplay of older people's food choices and meal patterns with gender, substance abuse (especially smoking) and activity (social, mental and physical) continues to be important with advancing years. The role of elders in enabling the value of traditional food cultural knowledge to be transmitted to grandchildren and the wider community should be acknowledged.

Key words: measurement of food choice, dietary patterns, food variety, food beliefs, food systems, ethnicity, gender, indigenous, Yin-Yang hot-cold concept, activity, eco-nutrition.

2.1 The relevance of food choice and food patterns with ageing

There is increasing evidence that food choice and the patterns with which the chosen foods are eaten can make a difference to elderly health. However, these aspects of food intake are often not measured and the nature of the available measures requires consideration. Ultimately, the understanding of food choices and eating patterns needs to inform food and nutrition policy for the aged, something that is emerging in national and international guidelines and policy. Any such policy will take into account the determinants, constraints and opportunities for physical activity and be expressed in terms of the optimal energy and nutrient densities of foods and beverages to be chosen and distributed between episodes of eating and drinking. The food system, food cultural settings, and health status and care system will always play a role as well in the final nature of food choice.

2.1.1 Measuring and assessing food choice and eating patterns – available options and integrals of diet

As with all questions, those to do with food choice and eating patterns with ageing, answers depend on measurement and assessment. The options available are limited and well-known. They may be self-reports or observations by others or a combination of these. In the case of older people, errors in reporting may be greater because of the influence of past habits on current representation of intake, cognitive impairment and dependency on others for foodstuff. Notwithstanding the difficulties, abbreviated and practical instruments for the nutritional assessment of the elderly are now available (Vellas *et al.* 1999; Olayiwola and Ketiku 2006; Bailey *et al.* 2007).

One of the challenges in this area is the lack of studies that have gathered information about food choices and eating patterns. These data should ultimately be treated in an integrated way with those about the foods and nutrients themselves. If not, the response to survey or study findings will be nutrient for nutrient or food for food and unlikely to be pattern for pattern, which may be the more important approach for the elderly community in question (Bjelakovic *et al.* 2007).

When it is considered that, depending on food culture, there may be significant diurnal variations in nutrient intake, with, for example, high intakes of thiamin and riboflavin from grains in the morning and of iron and zinc from red meat in the evening, health relevance is likely (Wahlqvist *et al.* 1999b). We know, for example, that assimilation of calcium into bone is better overnight than during the day (Eastell *et al.* 1992). The spread of food across the day is also relevant to glycaemic and insulin responses.

Again, a pattern of eating, as with the conjoined consumption of basic food commodities, may be lost or not captured in some data sets, e.g., vitamin C containing fruits, with iron containing breads or breakfast cereals; yoghurt and fruit with anti-hypertensive potential; culinary herbs and meats to provide pre-

ingestion anti-microbial or anti-oxidant food safety; soups, casseroles, stir fries to provide enhanced vegetable variety for phytonutrient adequacy and spectrum and, in particular, opportunity to increase legume intake which is associated with longevity (Darmadi-Blackberry *et al.* 2004).

That characteristics can be represented by simple and predictive mathematical expressions is evident from the FHILL (Food Habits in Later Life) studies (Wahlqvist *et al.* 1995a, 1995b; Wahlqvist and Kouris-Blazos 1999) of an integral of the Greek diet, as it was in Crete in the 1950s, and longevity amongst older individuals (Kouris *et al.* 1991; Kouris-Blazos and Wahlqvist 1998; Kouris-Blazos *et al.* 1996; Trichopoulou *et al.* 1995a, 1995b). This also applies for the FHILL studies across cultures (Darmadi-Blackberry *et al.* 2004; Kouris-Blazos *et al.* 1999) for the SENECA (Survey in Europe on Nutrition and the Elderly: a Concerted Action) (de Groot *et al.* 1991; Osler and Schroll 1997) scheme and other studies (de Lorgeril *et al.* 1999; Redondo *et al.* 1997; Lasheras *et al.* 2000). They can also apply in larger studies, like EPIC (European Prospective Investigation into Cancer and Nutrition) to the prediction of specific disease outcomes (Trichopoulos *et al.* 2003).

2.1.2 Relevance of food choice

There are many factors that may influence food choice, some of them demographic, others socio-cultural, economic, to do with skill base, physical and medical status and psychological and emotional factors (Darnton-Hill *et al.* 2002).

An interesting finding by Kouris and Wahlqvist, amongst older people of Greek ethnicity in Greece and Australia, was that belief could be strong and practice weak (Wahlqvist *et al.* 1991b). This may in itself not be so surprising, but the inter-generational persistence and enhancement of beliefs does seem to have a community and parent-child-grandchild value beyond its immediate food practice (Wahlqvist and Kouris-Blazes 1990). It is also striking amongst the Chinese diaspora, no matter how many generations, that food binds them together. It is not uncommon, in the Chinese restaurants of the world's Chinatowns, that the grandparents, especially the grandmother, are present along with the grand children. This constitutes a setting for inter-generational food belief and practice education. However, surrogates for the original Chinese food creep in like the substitution of Coca-Cola for Chinese tea (Hsu-Hage and Wahlqvist 1996). Like the Greek elders, some of the food cultural transmission is somewhat virtual rather than real!

Food choice, often predicated by socio-economic and food systems, plays a significant role in body compositional disorders in the aged (Wahlqvist *et al.* 1995c). For the same body weight, there can be more or less of any body compartment, namely fat mass or lean mass (muscle, organs, bone, blood), with profound differences in health status. The findings in Korean elderly (Park *et al.* 2003) show that low BMI, which equates with chronic energy deficiency, low energy intake and micronutrient deficiencies are commonly associated, especially

in low income groups. This indicates that eating enough food, by energy criteria, and which is sufficiently nutrient dense (essential nutrients per unit of energy) is crucial. The reverse is also true; that excessive energy intake from foods of high energy density (amount of energy per unit of food mass) and low nutrient density, especially with little resistance activity for strength, will be associated with sarcopenia and adiposity at the same time (Wahlqvist *et al.* 1995c). The problem may be even more impressive in the case of vitamin D deficiency, where sunlight exposure can be critical and missing or avoided (Wahlqvist and Lee 2007), because of the role of vitamin D in muscle function and in bone health.

2.1.3 Relevance for food patterns

Food choice and patterns may have their origins in the remote cultural past and be retained as an expression of heritage and tradition, and as a method of maintaining social cohesion – an aspiration of community leaders and many elders. The Chinese language goes so far as to distinguish between foreign and original foods (Wahlqvist and Lee 2007) (Table 2.1). This may have occurred despite the original logic for the choice or pattern no longer being applicable. It has, perhaps, to do with safety such as with shell-fish and pork in Halal and Kosher traditions or availability, for example again, as with pork in oriental traditions, but also seeds and berries in Scandinavian traditions, and dairy with herds-people. Some determinants of food choice and pattern are, understandably, enduring and evolving, such as: ease and nature of living (e.g., shopping, cooking, meeting others, means of gainful employment) and adjustments to health needs (e.g., insulin resistance syndrome and meal size; incontinence, both urinary and faecal; medication).

Recently, national dietary guidelines for the elderly have started to appear, as in Australia (Darnton-Hill *et al.* 2002). Globally, the WHO (World Health Organization) has taken FBDGs (Food-Based Dietary Guidelines) (World Health Organization, 1998) a step further, with specific reference to the aged (World Health Organization, 1998, 2002; Wahlqvist *et al.* 2002).

All such guidelines champion the combination of physical activity to allow enough food to be eaten, and food variety to enable food component needs to be met adequately and comprehensively (Wahlqvist *et al.* 2001a; Savige *et al.* 2001). It is hoped that such guidelines influence health policy makers, carers, and the elderly themselves to adjust their food choices and patterns in favourable directions (see Table 2.2). They also address specific needs like fluid intake with decreased thirst sensitivity and nutrient density for dietary fibre or calcium, whilst neglecting growing concerns about vitamin D, folate, vitamin B-12, and n-3 essential fatty acids in particular (unless addressed by the combined recommendations of food variety and physical activity). They have a basis in chronic disease prevention strategies as well – cardiovascular disease, diabetes, cancer, osteoporosis, impaired cognitive function.

Systematic population-based studies point to growing concern amongst older people as to the adequacy of their diets, as dietary supplement usage increases

Table 2.1 Representation of origin of foods by Chinese vocabulary

English	Chinese /pronounce/	Meaning	Other example
Onion	洋蔥 /yang cong/	洋 foreign, especially Western	洋芋 (potato)
Pepper	胡椒 /hu jiao/	胡 introduced or imported into China proper in ancient times	胡瓜 (cucumber); 胡蘿蔔 (carrot)
Sweet potato	蕃薯 /fan shu/	蕃 uncivilised; foreign	蕃茄 (tomato); 蕃麥 (corn)
Water melon	西瓜 /xi gua/	西 west; Western	西紅柿 (tomato)

progressively, especially amongst older women. In the NHANES (National Health and Nutrition Examination Survey) studies from 1971–74 to 1999–2000, amongst 60–74-year-old US men this usage increased from 32 to 61% and in US women from 40 to 66% (Briefel and Johnson 2004). Food choices and patterns are likely to reflect these attitudes; the more concerned about supplements may actually have the healthier diets in the first place (Wahlqvist *et al.* 1988).

The interplay between health needs, perceived or real, and food patterns can become a matter of complexity and concern with advancing years. Preventive nutritional measures for adults in recent years have focussed on macrovascular disease (MVD) and other so-called 'chronic diseases' (obesity, diabetes, osteoporosis, certain cancers). Unfortunately, the understanding of the pathways linking diet and MVD was relatively narrow (notably located around hypertension and lipoprotein disorders) when the present generation of elders was the target of such public health nutrition as younger adults. People paid much attention to reducing saturated fat, cholesterol and sodium and increasing dietary fibre intakes. Typically, meat, dairy products and eggs were restricted and

Table 2.2 Dietary guidelines for elderly Australians

1. Enjoy a wide variety of nutritious foods.
2. Keep active to maintain muscle strength and a healthy body weight.
3. Eat at least three meals every day.
4. Care for your food: prepare and store it correctly.
5. Eat plenty of vegetables (including legumes) and fruit.
6. Eat plenty of cereal, breads and pastas.
7. Eat a diet low in saturated fat.
8. Drink adequate amounts of water and/or other fluids.
9. If you drink alcohol, limit your intake.
10. Choose foods low in salt and use salt sparingly.
11. Include foods high in calcium.
12. Use added sugars in moderation.

Source: National Health and Medical Research Council Australia

dietary fibre was added to products as an ingredient. The more food-based and food pattern approach was yet to come (Wahlqvist and Dalais 1999; Wahlqvist and O'Brien 1993) which encouraged food variety, an emphasis on plant-derived foods, unrefined fats from relatively intact plant sources (grains, nuts and other seeds and fatty fruits, fish, lean unprocessed muscle and organ meats in small quantities, low fat dairy products like yoghurts and eggs cooked without animal or hydrogenated fats, e.g., boiled, poached, scrambled with low fat milk). It came to be recognized that vascular and cardiac health were dependent on many food components, especially n-3 fatty acids, arginine in protein from plant sources like nuts, and polyphenolic phytonutrients, in addition to micro-nutrients with cardiovascular relevance, like vitamins B-6, B-12 and folate.

In the meantime, the exclusion of nutritious foods like eggs, lean meat, liver and nuts from the diet by older people in the belief that this would reduce cardiovascular risk, has made it more difficult for them to achieve nutrient adequacy. In some, as documented by Clarke and Wahlqvist (Clarke *et al.* 1998, 1999) this has contributed to 'disordered eating' patterns (DEP). DEP can also occur because of the immediate priority needs of symptom control – especially with urinary and faecal incontinence. Here, fluid balance as well as nutrient adequacy may be compromised (Clarke *et al.* 1998).

Inappropriate restricted eating may also be seen in efforts to manage weight rather than body composition (muscle, fat, bone, fluid), and fitness (Wahlqvist *et al.* 1995c, 2001a; Savige *et al.* 2001). Body mass indices in the 'overweight' range, approaching 30 kg m^{-2}, are not associated with reduced life expectancy in the aged (Blackberry *et al.* 2004; Wahlqvist *et al.* 2005a). However, this is not to say that excess body fatness is not associated with morbidity in the aged – reduced mobility, falls, cardio respiratory impairment, diabetes and its complications. Dealing with these through restricted food patterns brings with it nutritional risks to do with nutrient adequacy, socialization and medication usage.

In order that enough food of available nutrient density can be eaten to satisfy nutritional needs, there must be sufficient energy throughput and this requires a metabolic rate significantly greater than that at rest – which means the human organism must be physically active for its survival, not surprising since mobility characterizes the species' very existence. Some idea of minimal energy needs for optimal health comes from a consideration of those movements needed to function as an individual, in a family unit, and in a community. At the very least these include ADL (Activities of Daily Living) and the ability to walk from one's place of rest to obtain food and to socialize, as evidenced in the FHILL Survival Studies (Wahlqvist *et al.* 2005a). The corollary of these observations for the aged is that as we age, we need to remain active and enjoy a variety of foods.

Where food variety has been measured as the number of biologically distinct foods eaten over a certain time frame (e.g., a week, a month, a year) (Wahlqvist *et al.* 1989; Hodgson *et al.* 1994; Hsu-Hage *et al.* 1996; Wahlqvist, 2003), and outcomes considered (Franceschi *et al.* 1995; Kant *et al.* 2000; Wattanapenpaiboon and Wahlqvist 2003), somewhere between 20 and 30 different foods, of

usual serving size in the culture in question, per week seems satisfactory. Advancing age, disinterest or limited access or disability could compromise achievable food variety.

2.2 Commonality and difference in eating

Later life is a particularly heterogeneous biological stage in the life cycle – much more so than infancy, childhood and adolescence. However, in general, biological age has been improving (is 'younger') at the same chronological age, and life expectancy has been increasing progressively in most socio-economically advantaged nations (Khaw 1997; Mathers *et al.* 2001). Food choice will, at least in part, have contributed to this biological heterogeneity amongst the aged which, in turn, will create different nutritional needs in the same chronological age group.

At the same time, peoples of apparently quite diverse food culture can achieve comparable life expectancies with minimal disability – examples would be Scandinavian, North East Asian, Mediterranean and the Dutch (Mathers *et al.* 2001; Wahlqvist 2003; Wahlqvist and Lee 2007). But the commonalties might be, for food, regular use of fish and legumes and a requisite food diversity, accompanied by physical activity (Darmadi *et al.* 2000).

2.2.1 An individual's food variety

The two most agreed principles of human eating are to optimize breastfeeding, ideally exclusive for the first six months of life (the current WHO guideline on breastfeeding) and, as growth and development continues, to diversify food intake amongst various biologically distinct food sources. Various studies point to the importance of food diversity in minimizing morbidity and increasing life span in later life (Horwath 1987, 1989; Horwath *et al.* 1999, 1992; Lee 2004). This is the nature of an omnivorous species which depends on a range of sources for substances essential or optimal for life (Horwath 1987; Lee 2004).

2.2.2 Food diversity within a community

Whilst the human species will have achieved a high level of food variety as hunter-gatherers, with the advent of pastoral and subsistence agricultural food systems, more restricted food patterns were likely. Indeed, Jarred Diamond (Diamond 1999) has observed that the range of seed crops cultivated by humans is only a dozen or so. More diversity may be obtained from horticultural produce – fruits and vegetables – with notable achievements in crop diversification in the Andes (Incas for potato), China and Taiwan, the Mediterranean and Africa.

Generally, communities need to be cooperative in food production, processing, storage and trade to achieve the required food variety. In such communities, food adequacy and nutritional value will be less vulnerable than

others, depending also on a host of material and personal resources and the systems of governance in place (Wahlqvist *et al.* 1999a). The elderly may be amongst the more vulnerable unless social organization recognizes their need for a varied food pattern. In Australia, socio-economic status is an important determinant of achieved food diversity and this will affect the aged (Wahlqvist *et al.* 2005b).

Of course, adverse seasonal or climatic conditions can compromise food variety within a community, with the most vulnerable at greatest risk. Some of this risk can be offset by food technology to keep food supplies available and varied despite the adversity. Again, this requires a reasonably developed economy and for the elderly to be a part of it (Wahlqvist 2006a,b).

2.2.3 Geographic and ethnic difference

Not infrequently, restricted food supplies stimulate migration and, with this the transfer and amplification of food diversity (Wahlqvist and Lee 2007). Successive waves of migration to Australia and other culturally pluralistic societies have had a major impact on food diversity, particularly with migration from the Mediterranean and Asia, especially of Chinese people (Wahlqvist, 2002). Owing to the Chinese, in particular, the whole Australian food system from production to trade to cooking and retailing has been affected. Many of today's elderly Australians have learned to cook in the Chinese 'wok' fashion because of the influx of Asian students from the 1950s onwards. Chinese Australians have the greatest food diversity of any ethnic group studied and their impact on the majority food culture is likely to have been the greatest. These are unintended but consequential phenomena affecting food security amongst older people (Wahlqvist and Specht 1998; Wahlqvist *et al.* 1999a).

It is possible for a food culture, and especially the potentially vulnerable within it such as the elderly, to manage with a narrow food diversity, if the foods chosen are sufficiently different one from the other and nutrient dense. There is a growing need for measures of this phenomenon as it presently exists and for its encouragement as required. Those cultures which have fish or unprocessed lean (fresh or frozen) meat, even in small amounts, along with plentiful and varied intact plant food, including legumes, generally fare better nutritionally (Darmadi-Blackberry *et al.* 2004). To evaluate these possibilities in food cultural terms reference can be made to Table 2.3 (Wahlqvist and Lee 2007).

2.2.4 Gender and its impact on food habits with ageing

It is increasingly recognized that the scene is set for life-long health by the nutritional status of our mothers and grandmothers (Solomons, 2005). There is little doubt that women, especially grandmothers are the principal custodians of food knowledge in a community, and that their literacy (including that of food) counts for the whole community. They also tend to make the nutritional decisions, even for supplements (Wahlqvist *et al.* 1988). That women generally

Table 2.3 Food systems by original location, ethnicity or characterizing foods: some examples

Locality of origin	Ethnicity	Characterizing foods or food production
• China (e.g., Cantonese, Yangtze delta, Hainan, Northern, Szechuan) • Japan • France (e.g., Provincial, Parisian, Coastal) • Africa (e.g., North-west, Nile Valley, Rift Valley, Kalahari Desert) • India (e.g., Chennai (Madras), Punjab, Bengal) • Indonesia • Andes • Scandinavian • Mediterranean	• Various indigenous people (e.g., Australian, Pacific Islands, Native Americans, Andean, Okinawans) • Chinese (in various locations – SE Asia, North America, Australia) • European (e.g., Italian, Greek, French, Swedish, German, Polish) • Russian • Minangkabau in West Sumatra; Bataknese in North Sumatra	• Hunter-gatherer • Subsistence agriculture • Rice-based (e.g., Asia) • Potato-based (e.g., Andes, Meso-American, Europe) • Wheat-based (e.g., Middle East, Europe, America) • Plentiful horticultural products (e.g., Tropical, Mediterranean) • Pulses (e.g., soy, beans) and leafy greens as a principal source of protein (South Asia, NE Asia, Meso and South America) • Fish (e.g., Islands, Coastal) • Meat (e.g., pork in China, beef in Argentina and USA, lamb in New Zealand, chicken in SE Asia)

outlive men is partly a reflection of their food and nutrition ascendancy over men. It also means that, in groups of oldest aged, there is a disproportionately high level of food belief and knowledge available to children and grandchildren, as long as the community does not disenfranchise these elders.

2.3 Regions

Most regions of the world became populated thousands of years ago by people who were firstly hunter-gatherers and later subsistence farmers. Only some of these communities have survived in a recognizable way. They can inform our understanding of the role of different age groups in the food system and how elders contribute to it and are affected by it. Region by region it is useful to gain an appreciation of contemporary and often disappearing food beliefs and habits. This section does this, but is limited by the general lack of studies that systematically address food and health amongst the aged by region.

2.3.1 Indigenous elders

Indigenous elders have only rarely been studied in regard to their food beliefs and habits (Wahlqvist *et al.* 1991a). One of the oldest and most continuous of indigenous cultures, but with a history of hundreds of different language groups and tribal groups, is that on the Australian continent, together with the Australian state of Tasmania, often referred to as Australian aborigines or Aboriginal Australians. Elderly indigenous Australians are the traditional spokespeople of the community with whom decisions or arrangements are made. Kouris, Wahlqvist and Gracey worked with the elders of several tribal groups in the Kimberly mountains and along the Fitzroy River to understand the role of food beliefs or culture for health (Wahlqvist *et al.* 1991a; Kouris-Blazos and Wahlqvist 2000). Even though the use of traditional foods may be as little as 10% of the total energy intake in those based in townships, the meaning and role of these foods in the sense of indigenous identity and continuity remains strong. The elderly play a key role through the knowledge of traditional food systems in the overall health and well-being of the community.

Examples of some Indigenous Australians foods and food habits are shown in Figs 2.1–2.5 (Kouris-Blazos and Wahlqvist 2000).

Bush foods were eaten at least a couple times a week prior to the 1960s. Bush foods made up more than 50% of total food intake at that time (in contrast to less than 20% in 1988). Bush fruits and bulbs (see Fig. 2.1) were eaten on a daily basis, except for bush watermelon and passionfruit which were not available. Also, nectar and pollen from flowers were regularly made into drinks. Seeds, however, were rarely collected and ground to make flour for damper. Men went hunting on weekends and women gathered bush foods daily. Kangaroo was

Fig. 2.1 Bush Onion *(Cyperus bulbosus).* Small plant with grass-like leaf and small onion-like bulb beneath, eaten raw or roasted in warm ashes (1 cm diameter). Ready to eat when grass on top turns brown, optimal time is during the wet season, but is available throughout year. Not eaten during the wet season because it causes nausea. Very popular with the elderly, but difficult to obtain because it is located in bush far away from Junjuwa. (Copyright permission from APJCN 2000; 9 (3): 224–231.)

Fig. 2.2 Bush Potato *(Vigna lanceolata)*. Ground creeper, roots eaten raw or cooked in hot ashes, small thin tuber, has sweet potato-like flavour. (Copyright permission from APJCN 2000; 9 (3): 224–231.)

eaten a couple of times a week and the following foods were eaten about once a week when available: wild cat, dingo, cockatoo, flying fox, echidna, snake, turtle, duck, yabbies (fresh-water crayfish), ant eggs, brown ants, manna, caterpillars, insect galls, duck and turtle eggs. On most days of the week mussels, witchetty grubs, grasshoppers, sand frogs, bush honey, tree gum, goanna and fresh water fish were eaten. About once a month bush turkey, emu and eggs, pigeon and crocodile were eaten.

In the 1980s bush foods no longer formed a major part of the Aboriginal diet in the Kimberleys – less than 20% of total food intake. The indirect impact of European settlement due to overgrazing has caused widespread pasture degradation and soil erosion – many plant foods have become rare and localized. This has been matched by a loss in native animals. Displacement by introduced animals has played a role here. Kangaroo is no longer found in the Fitzroy Valley region. Elderly Aborigines in 1988 consumed bush foods about once a month. The most commonly eaten native foods were bush gooseberries (*Physalis peruviana*), bush passionfruit, cucumbers, river figs (*Ficus coronulata*), conkerberries (*Carissa lanceolate*), onions (*Cyperus bulbosus*), bush sweet potato (*Vigna lanceolata*) (Fig. 2.2), tree gum, honey, fresh fish (barramundi, black bream), cherrabun (fresh-water crayfish), mussels, goanna (native lizard) (Fig. 2.3) and sand frogs. The traditional indigenous cooking method of an open fire or hot coals and stones for hunted and gathered foods is these days applied to wheat flour and water to make a kind of unleavened bread called damper (Figs 2.4 and 2.5).

In Taiwan, the food habits of indigenous people have been documented as part of the Nutrition and Health Survey in Taiwan (Elderly NAHSIT) and are incorporated into the main report (Chen *et al.* 2005).

Fig. 2.3 Older Aboriginal Australian successfully traps a goanna (native lizard) in the bush; goanna taken back to Junjuwa where it is cooked on the ashes and shared with grandchildren and the investigators (Professor Wahlqvist far right). (Copyright permission from APJCN 2000; 9 (3): 224-231.)

2.3.2 Europe

The longitudinal Survey in Europe on Nutrition and the Elderly: a Concerted Action (SENECA) study, has documented food cultures of elderly people across the European continent (de Groot *et al.* 2004). The SENECA programme was designed to assess differences in dietary and lifestyle factors among elderly from Belgium, Denmark, France, Italy, Portugal, Spain, Switzerland and The Netherlands, and to identify the factors that contribute to healthy ageing. Standardized measurements were conducted at baseline in 1988–1989 and were repeated in

Fig. 2.4 Cooking damper (unleavened bread) in the bush; white flour is mixed with water on a piece of cloth and kneaded into a dough and flattened into a thin pita style bread; covered with ashes and allowed to cook for about 20 minutes. A wire rack was sometimes placed over the coals of an open fire to cook damper or meat; a small pot 'billy can' was used to make tea and meat stews. (Copyright permission from APJCN 2000; 9 (3): 224–231.)

1993 and 1999. Diet, physical activity and smoking as well as maintenance of health and survival were assessed.

At baseline, considerable differences in lifestyle factors existed among elderly people. Mealtime patterns as well as dietary intake varied across Europe, and geographical patterns were apparent. Similar results were found for engagement in sport or professional activities with smoking prevalence among women being generally low. Distinct geographical differences were also observed in percentages of deaths during the SENECA study and in overall survival time. A healthy lifestyle was related to stable self-perceived health, a delay in functional dependence, and mortality. Inactivity and smoking, and to a lesser extent a low-quality diet, increased mortality risk. A combined effect of multiple unhealthy lifestyle factors was also observed. The SENECA study showed that a healthy lifestyle at older ages is related to a delay in the deterioration of health status and a reduced mortality risk. This fact is underpinned by Knoops *et al.* (2004) who combined data with the FINE study.

Fig. 2.5 Investigators weighing fried damper to determine average portion sizes consumed by the elderly; cooking damper (unleavened bread) at home; dough is flattened and then fried in an electric fry pan in oil or margarine (known as Johnny cake) as this is easier and faster than cooking it in the ashes of a fire. White damper is preferred to wholemeal because it was reported to taste better, was easier to chew and thought to be 'lighter'. (Copyright permission from APJCN 2000; 9 (3): 224–231.)

2.3.3 North Eastern Asia and Africa

Extensive information about North East Asian elderly persons (China, Korea and Japan) is available through the FHILL studies (CD-Rom) (www.healthyeatingclub.org/APJCN/FHILL/index.htm) (Wahlqvist *et al.* 1995a). However, the rapid changes in the demography of ageing in the Asia-Pacific region requires much greater attention (Lee and Wahlqvist 2005).

There has been an effort in Africa to document at least some of the local food habits in regard to ethnicity (Charlton *et al.* 2001) and with special reference to aid programmes like HelpAge and Oxfam. These observations and programmes are highly relevant for communities affected by HIV-AIDS where elders often become the carers of grandchildren otherwise orphaned. The healthy eating club (HEC) has a programme to encourage an understanding of African food cultures because of their global importance in the origin of foods and food habits, as a step towards their greater role in community health advancement (www.healtheatingclub.org/africa).

2.3.4 Other areas

There is still a great deal more to know about South Asia, Central Asia, South East Asia, the Middle East, Eastern Europe, Russia, South America and the Pacific Islands. As populations age, so regard for their traditional food cultures and how they adapt to a changing world food supply will be important for sustainable health patterns. The focus of the present review of food and the elderly is not only how this relates to mortality and disability, but also to wellness and well-being through food-related body composition, body mechanics, cognitive function, immune function and mood, each of which is at the very early stages of enquiry. The indications from a study of elderly Guatemalans (Herman *et al.* 2001) are that there is much to be realized in regard to wellness.

2.4 The example of Chinese-speaking people

A common Chinese saying is 'Vegetables and tofu can ensure your health'. This might be expected to continue to inform recent and current generations of elderly Chinese in regard to their eating habits. However, the importance of other factors in food choice is evident from various observations.

One is a past history of privation, particularly evident during the Sino-Japanese wars and the Japanese colonization of Taiwan for some 50 years until the end of World War II. People in Taiwan mainly ate sweet potato during World War II. Since then the mantra has been '*Si Tsai Yi Tang*' meaning 'Four food dishes and one bowl of soup'. With this practice, a typical meal (one meat, two half-meat-half-vegetable and one pure vegetable dishes) includes both animal and plant food sources, as well as solids and liquid. At the same time, this meal structure can provide for dietary diversity. Such a meal is best suited for family. The components are relatively unchanged with age (Wu *et al.* 2005), but there is relatively more emphasis on fish than meat, and on vegetables and fruits. This is seen in both the eight provinces study in China from 1989 to 1997 in the 60+ years group (Luo *et al.* 2001) and the Elderly Nutrition and Health Survey in Taiwan (NAHSIT) in 1993–1996 and 1999–2000 (Wu *et al.* 2005).

The overall achieved nutrient density of a low energy diet can depend on small quantities of animal-derived foods of which eggs are an example. In various parts of Northern China egg (and other foods) consumption depended on the overall food culture and tradition – pastoral (Tuoli and Xinyuan), fishing (Baoshan and Rongcheng), agriculture (Huairou) or urban (Beijing) (Zhao *et al.* 1995). But, generally, elderly Chinese people have managed to eat an average of a half to one egg a day in various socio-economic circumstances. It is a nutritious item, but, more evidently in Taiwan, its consumption has decreased amongst the elderly (as in the West) on account of successful public health nutrition campaigns directed at the links between diet and coronary heart disease. In these campaigns, regard has scarcely been given to the nutritional

needs of elderly people for foods of high nutrient density (like eggs) or of investigating dietary factors like how the egg is cooked or eaten, or what the nutritional priorities of the life stage in question are.

2.4.1 Yin-Yang and hot-cold food concepts

The '*Hot and Cold Concept*' of food choice, linked to Yin-Yang philosophy, is widespread throughout North East and South East Asia. Unpublished observations, by Chen Chun-Ming, Motoko Sakamoto and Mark Wahlqvist, indicate that the epicentre of this belief system is China with strong representation (most of the population adhering to it) in Japan, Taiwan and Korea as well. The belief system is diluted in South East Asia, largely depending on historic Chinese influence, as in Thailand, the Philippines, Malaysia, Singapore and Indonesia. It remains to be seen how robust the belief system will be in future generations, but, for the moment, the elderly adhere to it and advise their children and grandchildren accordingly. It is relevant at every stage of life, from menstruation and conception to lactation, infant feeding, growth and development, and ageing to education, incidental illness, mood and well-being. There are now repositories of information about 'hot and cold foods' on web sites (http://www.shen-nong.com/eng/lifestyles/food_property_food_tcm.html), but some examples, which are considered to modulate 'the body's energy', are shown below:

'Energy generated' – Examples of food

Yin – Cold

Bamboo shoot, banana, bitter gourd, clam, crab, grapefruit, kelp, lettuce, muskmelon, persimmon, salt, sea grass, seaweed, water chestnut, watermelon and lotus root.

Yin – Cool

Cucumber, apple, barley, bean curd, egg white, common button mushroom, eggplant, lily flower, mandarin orange, marjoram, mung bean, oyster, pear, peppermint, radish, sesame oil, spinach, strawberry, tangerine, wheat, wheat bran, cream, yogurt and cheese.

Balanced Yin and Yang – Neutral

Corn, abalone, apricot, beef, beetroot, black sesame seed, black soybean, cabbage (Chinese), carp, carrot, celery, egg yolk, cuttlefish, dry mandarin orange peel, duck, fig, grape, honey, kidney bean, licorice, lotus fruit and seed, milk, olive, oyster, papaya, peanuts, pineapple, plum, rice, pork, potato, pumpkin, red bean, Japanese mushroom, sunflower seed, sweet potato, taro, sugar, yellow soybean.

Yang – Warm

Chicken, brown sugar, carp, cherry, chestnut, chive, cinnamon twig, clove, coconut, coffee, coriander, date, dill seed, eel, fennel, garlic, ginger (fresh),

ginseng, green onion, guava, ham, kumquat, leaf mustard, leek, litchi, longan, mutton, nutmeg, peach, raspberry, rosemary, shrimp, squash, star anise, sweet basil, vinegar, walnut, wine.

Yang – Hot
Pepper, cinnamon bark, cottonseed, ginger (dried), soybean oil, red and green pepper.

The notion is not one of food temperature, but the state of one's body, especially lining tissues (skin, mucous membranes) and how one feels, which may include feeling hot or cold. A 'hot food' will tend to counteract the effects of a 'cold food' and vice versa. Achieving a balanced relationship between these categories in different physiological and health situations is the goal of food choice. A 'hot food' may, for example, lead to a dry mouth and mouth ulcers, constipation and haemorrhoids. A 'cold food' may make hands and feet cold and pale; it can increase vaginal discharge.

Food and nutrition scientists are beginning to find common compositional characteristics between hot and cold foods. For example, Ni and Rao of Fuzhou University in China have demonstrated a close association between the Mg/Cu ratio of a food and its alleged 'hotness' or 'coldness' (Ni *et al.* 2007). Huang Ching-jang and colleagues of the National Taiwan University have demonstrated characteristic prostaglandin production profiles of foods traditionally classified as 'hot' or cold' (Huang and Wu 2002). It seems likely that such an ancient and enduring food belief system will have some underlying mechanistic basis. In the meantime, for many of the world's elderly, it is the most important determinant of food choice.

2.4.2 Successful ageing and difference amongst Chinese

Fortunately, successful ageing amongst Chinese and other peoples appears possible with various food sub-cultures and belief systems. Nevertheless, food variety or diversity is associated with less micronutrient (and inevitably phytonutrient in general) deficiency (Lee 2004), less cardiovascular risk (hypertension, dyslipidaemia and abdominal obesity) and less of the metabolic syndrome and risk of diabetes (Hsu-Hage and Wahlqvist 1994, 1996; Lee 2004).

The gender differences in food consumption with age amongst Chinese may ultimately confer biological advantage on women over men (Horwath *et al.* 1999). They include more fruit and vegetables and less meat, which may represent gender preference, but may also reflect pressures on intra-household distribution (Luo *et al.* 2001) according to the 'Contribution rule' (those in the family with the greater apparent economic contribution receive a larger share of food energy). The 'Contribution rule' is under challenge insofar as male gender favouritism is concerned, but may still be adverse for older people.

It is of interest that elderly Chinese women do tend to increase dairy consumption when this is possible, probably in response to health messages and

concern about calcium intake and osteoporosis (whatever its validity in China where other factors may be more important for bone health) (Lau *et al.* 1998). Yet it is the major missing food category in the Taiwan NAHSIT II dietary diversity score (DDS) which, as it increases, is associated with less dietary deficiency and less risk of cardiovascular disease and diabetes (Lee 2004).

2.5 Conclusions and policy implications

As the 'Okinawa round-table' (Wahlqvist *et al.* 2001b) on nutrition and cardiovascular disease in the Asia Pacific region demonstrated, a regional and cultural view of food-health relationships is required, not only to avoid the mis-transfer of concepts about food and health, but also to open new possibilities for their contribution to human populations.

There are extensive and substantive differences in the way older people eat, much of it based on demography and culture. Some life-long food beliefs and habits are retained into later life and will have contributed to survivorship. Within or between communities, there remains heterogeneity in residual survivorship, disability and well-being. Evidence grows that the differences in food intake can contribute to the differences in health status, and that, with effective food and health policy, progressive health gains can be made (Wahlqvist *et al.* 2002; World Health Organization 2002). In any case, we are presently witnessing some of the greatest gains in disability-adjusted life expectancies (DALES) ever made in human history, at a time when nutrition science and policy is undergoing a revolution. At the same time, there have been disturbing limitations in public health nutrition policy during the late 20th century through poor appreciation of food–health relationships, which can now be rectified, but not without a commitment to constant review and revision in strategy. The core policy for nutrition and the aged is, however, likely to remain adequacy and diversity of food intake along with regular physical activity of various types (aerobic, strength, balance and flexibility) (Savige *et al.* 2001; Wahlqvist *et al.* 2001a), with good local governance (Wahlqvist *et al.* 1999a) and sustainable food systems (Wahlqvist and Specht 1998; Wahlqvist 2006a, 2006b).

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3

Appetite and ageing*

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Abstract: This chapter discusses the regulation of food intake control in the elderly and tries to depict the characteristics of anorexia of ageing. The chapter first reviews the determinants of food choice, the CNS control on food intake and the biomarkers of appetite. The chapter then discusses the definition and classification of senile anorexia, its epidemiology and its pathogenesis. Anorexia of ageing is therefore classified as physiological (related to disruption of CNS or gastrointestinal control, to altered peripheral feed back signals or to food variety and hedonic qualities of food), pathological, iatrogenic or related to environmental and psychological causes.

Key words: anorexia of ageing, food intake, biomarkers of appetite.

3.1 Introduction

Food influences human well-being and quality of life. In fact, its influence extends not only beyond the simple satisfaction of hunger and provision of energy and nutrients, but it may also assume a symbolic meaning relating to religious, cultural, social and emotional experiences, which may determine food habits. Moreover, food influences independence and self-esteem because of the relationship between physical and mental functions and nutritional status (Shepherd & Mela, 1999).

Food also has a special significance in the final stage of life. Indeed, elderly people who show an interest in food and nourishment and retain a good appetite, are, in most cases, still vital human beings, quite independent and with many

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interests – all qualities that characterise *successful ageing* (Rowe & Kahn, 1987).

Ageing is normally associated with changes in body composition, such as weight gain, specifically in individuals who fail to decrease their food intake in proportion to an age-related reduction in energy expenditure. However, decreases in body weight are also very common in the elderly (over 70 years of age) who do not eat enough to meet their energy demands; in Western countries especially, the elderly population is the single largest demographic group at risk of an inadequate diet and malnutrition (Rolls, 1992).

Little information is available about how energy requirements change with age, particularly for people of over 74 years of age, and there is no general consensus on the desirable range of physical activity (the major determinant of variability in total energy expenditure), and hence energy requirements (Roberts, 1996).

Age-related reduction in energy intake is largely a physiological effect of ageing and manifests itself in a loss of both the need to eat and the pleasure in eating. Psychological, social or physical problems that become increasingly frequent with ageing may also contribute to the physiological reduction in food intake and predispose to malnutrition (Morley, 2001a).

In the elderly, a 10% loss of body weight over 10 years, generally recognized as a pathognomonic sign of malnutrition (whether energetic or protein-energy), is consistently associated with increased mortality and functional disability (Horwitz *et al.*, 2002). In particular, malnutrition may negatively influence the clinical outcomes of rehabilitation programmes, confirming that an adequate nutritional status is absolutely essential when recovering from acute illnesses (Gazewood & Mehr, 1998).

A further demonstration of the importance of nutritional status has been highlighted by several studies showing that, after the age of sixty, weight loss is associated with a decline in muscle mass and consequently in muscle strength. Sarcopenia may also affect the obese elderly, who are more often disabled due to a reduced capacity for rehabilitation, and for this reason they are described as the so-called *fat frail* (Stevens, 2000).

3.2 Regulation of food intake control

The brain receives and integrates a variety of signals which are important for maintenance of adequate energy stores. Adiposity signals such as insulin and leptin act in the hypothalamus, and this in turn determines the sensitivity of the individual to satiety signals influencing how much food is eaten at any time (Woods, 2005).

Humans appear to have a genotype permitting, or even encouraging, an energy intake level that is greater than energy expenditure when food is available. The above-mentioned system was functional throughout most of human evolution but is less so in the current environment, in particular in

Western countries. The mechanisms linking energy intake and expenditure are still unclear, but it seems that appetite (sensations that promote food ingestion or rejection) is central to the maintenance of energy balance (Mattes *et al.*, 2005). The disruption in the relationship between energy intake and expenditure accounts for the positive energy balance leading to obesity epidemics in Western countries and to the risk of malnutrition affecting the elderly populations.

In this view, a failure to monitor and appropriately react to internal appetite cues or a dysfunction in the present environment may influence the imbalance between energy intake and expenditure. Moreover the mechanisms regulating hunger, satiation and satiety have a physiological basis but may be strongly influenced by environmental factors or cognitive issues. Therefore there is a need for a greater understanding of the reasons of food choice.

3.2.1 **Food choice** (Table 3.1)

It is generally recognized that food choice may be affected by biological determinants such as hunger, appetite and taste, by economic elements (cost, income, availability), structural determinants (access, education, cooking facilities, skills and time), social characteristics (culture, family, peers and meals patterns) attitudes, beliefs and knowledge about food (EUFIC, 2005).

Humans need energy and nutrients in order to survive and will respond to the feelings of hunger and satiety (satisfaction of appetite, state of no hunger between two eating times). The balance between hunger, appetite stimulation and food intake is regulated by the central nervous system. The macro-nutrients i.e. carbohydrates, proteins and fats generate *satiety signals* of varying strength.

Table 3.1 Food choice determinants

- Biological determinants
  - satiety signals (macronutrients, energy density of diets)
  - palatability (taste, smell, texture, sound and sight)
- Economic elements
  - cost and income
  - availability
- Structural determinants
  - access
  - education
  - food variety
  - cooking facilities
  - skills
  - time
- Social characteristics
  - culture
  - family
  - peers and meals patterns
- Attitudes, beliefs and knowledge about food
- Psychological determinants (stress, mood)

Fat seems to have the lowest satiating power, whereas protein has been found to be the most satiating and carbohydrates have an intermediate effect (Stubbs *et al.*, 1996). On this subject, the energy density of diets has been shown to exert potent effects on satiety; low energy density diets generate greater satiety than high energy density diets.

Palatability

Palatability may influence food choice as it is proportional to the pleasure someone experiences when eating a particular food. It depends on the sensory properties of the food such as taste, smell, texture, sound and sight. In particular sight allows evaluation of food shape, dimension, colour that are qualities of food that can generate expectations of odour, freshness, texture, temperature, maintenance, edibility (Schiffman & Graham, 2000). It is well known that food intake increases proportionally to palatability, but the effect of palatability on appetite in the period following consumption is still unclear. Increasing food variety can increase food and energy intake, too, and in the short term it may alter energy balance (Sorensen *et al.*, 2003), while effects in the long term on energy regulation are unknown.

Taste

Taste is consistently reported as a major influence on food behaviour and, in particular, spontaneous food choice. In reality 'taste' is the sum of all sensory stimulations that are produced by the ingestion of a food: not only taste *per se* but also smell, appearance and texture of food. In particular, a liking for sweetness and a dislike for bitterness are considered innate human traits (Steiner, 1977). Moreover taste preferences and food aversions develop through experiences and are influenced by attitudes, beliefs and expectations (Clarke, 1998).

Psychological stress

This can modify eating behaviours and food choice. The effect of stress on food intake depends on the individual, the stressor and the circumstances. When experiencing stress, some people are not able to rationally control their food intake, they fall prey to unrestrainable emotions and so they may eat more (with the possibility of weight gain and consequently cardiovascular risk) or less than normal (Oliver & Wardle, 1996). Some of the proposed mechanisms for stress-induced changes in eating and food choice are motivational differences (reduced concern about weight control), physiological (reduced appetite caused by the processes associated with stress) and practical changes in eating opportunities, food availability and meal preparation (Wardle *et al.*, 2000). Food also influences our mood, and mood has a strong influence over food choice. Interestingly, it appears that the influence of food on mood is related in part to particular nutrients (e.g., PUFA and Zn) (Levenson, 2006; Parker *et al.*, 2006). Many people experience an ambivalent relationship with food: on the one hand they want to enjoy it while eating, but on the other hand they realize that it may lead to weight gain (Dewberry & Ussher, 1994). Moreover attempts to restrict

intake of certain foods can increase the desire for these particular foods, even leading to food cravings.

3.2.2 Central nervous system control on food intake (Fig. 3.1)

The central feeding system is influenced by the stimulatory effect of neurotransmitters including opioids, noradrenaline, neuropetide Y (NPY), orexins, galanin and ghrelin and by the inhibitory effect of corticotrophin-releasing factor, serotonin, cholecystokinin (CCK), cocaine-amphetamine-regulated transcript (CART) and possibly insulin (Chapman, 2004).

In particular, the *opioid feeding drive*, mediated in particular by dinorphin (but also by beta-endorphins and enkefalins), plays an important role in driving fat intake in animals and humans, in determining food palatability and in initiating and terminating eating. The central feeding drive may also be influenced by NPY, the most potent orexigenic agent, synthesized in the peripheral nervous system and brain. The effects of NPY are predominantly on foods rich in carbohydrate and strictly correlated to the actions of leptin, with each inhibiting the effect of the other.

A great importance is attributed, as a CNS control mediator, to *ghrelin*. This is a hormone produced, not only in the A cells of the stomach, but also in the

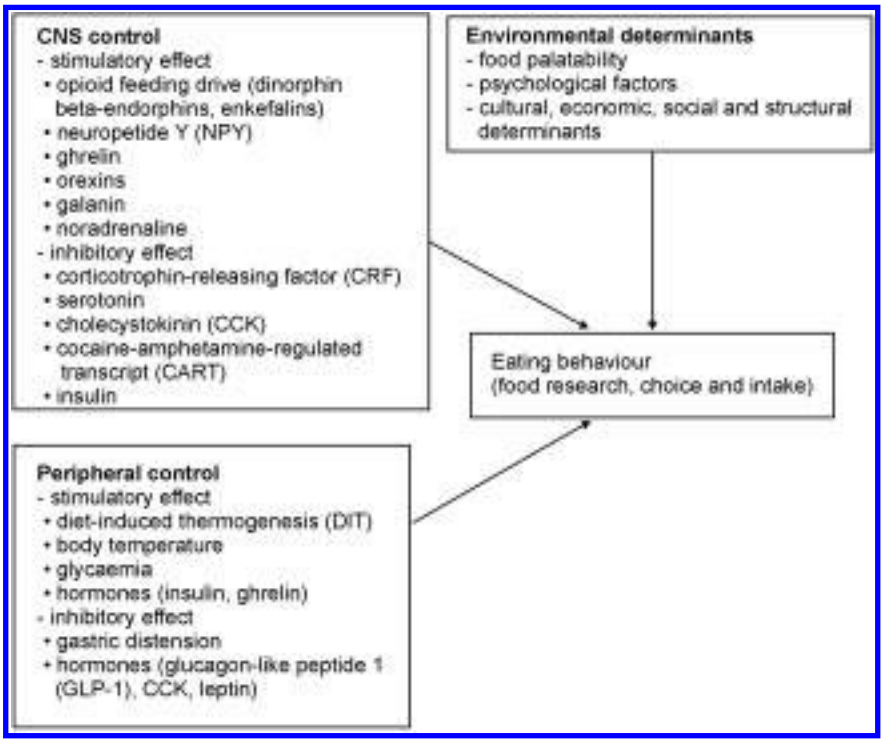

Fig. 3.1 CNS, peripheral and environmental control on food intake.

hypothalamus (in an area adjacent to the third ventricle, between the dorsal, ventral, paraventricular, and arcuate hypothalamic nuclei, where uncharacterized groups of neurons are localized (Smith *et al.*, 2005). This kind of neuron sends efferent signals to key hypothalamic circuits, which include those producing NPY, agouti-related protein (AGRP), proopiomelanocortin (POMC) products, and corticotropin-releasing hormone (CRH). In the hypothalamus, ghrelin binds mainly to presynaptic terminals of NPY neurons. Electrophysiological recordings show that ghrelin stimulate the activity of arcuate NPY neurons and mimic the effect of NPY in the paraventricular nucleus of the hypothalamus (PVN). Ghrelin, at these sites, stimulates the release of orexigenic peptides and neurotransmitters, thus representing another regulatory circuit controlling energy homeostasis (Sun *et al.*, 2004; Chen *et al.*, 2004).

3.2.3 Peripheral biomarkers of appetite (Fig. 3.1)

Peripheral satiation biomarkers which stop feeding include gastric distension and hormones (CCK, glucagon-like peptide 1 – GLP-1) (Cummings & Overduin, 2007). Satiety biomarkers that induce feeding are food-induced thermogenesis, body temperature, glycaemia and also several hormones such as insulin, leptin and ghrelin. Oxidative metabolism/body composition, tryptophan/serotonin and proinflammatory cytokines are also implicated in hunger physiology (De Graaf *et al.*, 2004).

Glucose

Glucose represents the basis of many short-term appetite regulation theories since the proposal of the glucostatic theory of eating in the 1950s (Mayer, 1953). Laboratory studies demonstrated that frequently a transient decline in blood glucose utilization precedes spontaneous meal request (Melanson *et al.*, 1999). Glucose, however, is not a robust measure of meal initiation. In fact meal requests frequently occur in the absence of transient declines in blood glucose and the association between transient glucose decline and meal requests disappears when subjects are in negative energy balance such as during an energy-restricted diet (Kovacs *et al.*, 2002). Thus the hypoglycaemia effect on appetite may be mediated by the correlated decline in insulin levels and its satiating role.

Ghrelin

Ghrelin has been identified as a potential biomarker of meal initiation. It is mainly produced and secreted by the gastric mucosa, stimulates food intake as well as GH secretion (Kojima *et al.*, 1999; Tschop *et al.*, 2000). Ghrelin increases feeding mainly in young, fast growing animals and therefore seems to link the high energy needs to body growth in young individuals (Gilg & Lutz, 2006). A clear pre-prandial rise in ghrelin concentration is followed by a rapid post-prandial decline (Cummings *et al.*, 2001). Its orexigenic properties are coupled with anabolic effects via the GH/IGF-I axis and the inhibition of the production of inflammatory cytokines. Ghrelin physiologically increases food

intake and stimulates adipogenesis, gastrointestinal motility and gastric acid secretion, and has other hormonal and cardiovascular functions (Milke, 2005). Energy intake has been observed to increase significantly even following intravenous ghrelin infusion (Wren *et al.*, 2001). Ghrelin may operate both in short- and long-term appetite regulation to correct an energy-deficient state. Its concentration was noted to rise in obese subjects who had lost weight (Cummings *et al.*, 2002).

CCK

CCK is probably the most important satiating hormone and is thought to be responsible for 20% of the signals leading to meal termination. It is released in response to the presence of fat or protein in the duodenum. It simultaneously causes the contraction of the gallbladder and the relaxation of the sphincter of Oddi. By this means bile is released into the duodenum, and pancreatic enzyme secretion is stimulated. CCK acts together, in a synergic way, with other hormones or neurotransmitters (serotonin, corticotrophin releasing factors, histamine, glucagons, somatostatin) and activates vagal afferent fibres that terminate in the brainstem. An increase in the contractile activity of the pylorus (slowing gastric emptying and increasing the sensitivity to gastric relaxation) mediates CCK effects. Stomach distension improves its appetite-suppressing effect (Kissileff *et al.*, 2003).

The regulation of the satiation system is under the control of the *adaptive relaxation of the stomach fundus*: dilatation allows it to act as a reservoir for food before passing along the antrum. In fact gastrointestinal sensory signals induced by relaxation of food contribute to initial sensations of fullness during a meal, and stomach distension is strongly associated with satiation and meal termination (Geliebter, 1988). It may be an adequate stimulus for satiation but it is not necessary. Some data demonstrate that meal volume is a more important determinant of meal size than energy or macronutrient content (Poppitt & Prentice, 1996). However, other studies reveal no association between gastric emptying and self-reported appetite (Lavin *et al.*, 2002). Artificial distension of the stomach by inflatable balloons decreases hunger (Geliebter, 1988) but tolerance to this manipulation develops quickly.

Nitric oxide

The production of nitric oxide (NO) (a short-lived gas produced by the endothelium, neuronal cells and inducible nitric oxide synthase) is correlated with the adaptive relaxation of the fundus stomach. NO, a transducer of the effects of a number of hormones in the control of feeding such as leptin and NPY, delays gastric emptying by altering pyloric tone and by modifying both receptive and adaptive relaxation of the fundus of the stomach to food.

Glucagon-like peptide l

GLP-1 is released predominantly in the ileum in response to the presence of nutrients. GLP-1 release influences gastrointestinal motility, insulin and

glucagon release and, through these mechanisms, may moderate appetite (Zander *et al.*, 2002). Its ability to reduce appetite has been demonstrated by studies that observed a 12% decrease in food intake following the infusion of this hormone (Flint *et al.*, 1998). Continuous infusion of GLP-1 over a six-week period results in decreased sensations of appetite and, more importantly, reduced body weight (Zander *et al.*, 2002; Hays & Roberts, 2006).

Leptin

Leptin, synthesized primarily by the adipose tissue, is responsible for appetite modulation, and provides information to the hypothalamus regarding the body's fat stores (Considine *et al.*, 1996). Elevated leptin levels, especially in men, may cause anorexia (Hays & Roberts, 2006).

Leptin seems to have a role in long-term energy balance, especially when energy balance is disturbed through under- or overfeeding (Weigle *et al.*, 1997; Keim *et al.*, 1998). In these situations, leptin correlation becomes very strongly correlated with hunger ratings (Heini *et al.*, 1998). Leptin effect on short-term eating behaviour is less clear. Leptin concentrations do not change reliably in response to a meal (Joannic *et al.*, 1998), although subjective ratings of hunger clearly do. Leptin is a peptide hormone belonging to the helical cytokines family (IL-6, IL-11, leukaemia inhibitory factor, ciliary neurotrophic factor). Further the leptin receptor is homologous to the signal-transducing molecule that it is also associated with the IL-6 receptor which activity decreases with ageing. Another mechanism whereby leptin inhibits food intake and stimulates energy expenditure involves altered transcription of hypothalamic neuropeptides (Green *et al.*, 1995; Licinio *et al.*, 1998). Leptin decreases orexigenic peptides expression (NPY, agouti-related peptide, melanin-concentrating hormone) and increases mRNA levels of anorexic peptides (propiomelanocortin, cocaine and amphetamine-related transcript).

Mutations identified in the leptin gene of rodents and humans are associated with altered metabolism and obesity (Farooqi *et al.*, 2001). Leptin secretion is subject to ultradian pulsatile rhythmicity, although the episodic profile is not as distinct as that illustrated by pituitary hormones. However, the pulsatile pattern becomes more organized at night, where fluctuations become synchronous with those of LH and estradiol (Licinio *et al.*, 1998). Leptin circadian and ultradian rhythms variations are inversely related to ACTH and cortisol rhythms (Licinio *et al.*, 1997; Licinio, 1998). Moreover *in vitro* studies have shown that leptin regulates biosynthesis of TSH releasing hormone, and studies on the synchrony of circadian/ultradian rhythms of TSH suggest that leptin also regulates TSH oscillations (Mantzoros *et al.*, 2001). Leptin decreases food intake and increases energy expenditure in rodents by inhibiting neurones in the hypothalamic arcuate nucleus (Traebert *et al.*, 2002). Ghrelin stimulates appetite and its receptor (GHS-R), like the leptin receptor (Ob-Rb), is expressed in the arcuate nucleus. Ghrelin interacts with the leptin hypothalamic network in the arcuate nucleus: leptin is inhibitory, and ghrelin increases the electrical activity in most of the cells that are inhibited by leptin (Traebert *et al.*, 2002). Hence, ghrelin

resistance can potentially be induced by an increased activity of leptin and leptin-receptor in hypothalamic neurons.

3.3 Anorexia of ageing

3.3.1 Definition and classification

Age-related anorexia may be defined as an unintentional decline in food intake that begins near the end of life, leading to body weight loss and represents a sign of a failure to preserve steady-state levels of body weight and energy stores. This phenomenon may be traced back to at least four reasons (Fig. 3.2):

1. *Physiological anorexia of ageing* is characterized by alterations at multiple levels of the food intake regulating system (as for example at: central feeding drive level, or peripheral satiation system and feedback signals from fat cells, absorbed nutrients and circulating hormones) and may be related to taste and olfactory acuity, dental status, physical activity.
2. Senile anorexia may occur in the presence of overt pathology (*pathological anorexia*). Decrease in appetite may be, for example, a symptom of worsening of serious illness (heart failure, pneumonia) or a consequence of disability (limitations in daily life activities, swallowing and gastrointestinal motility disorders). In other cases anorexia may be caused by increased resting energy expenditure, elevated cytokines and muscle and fat wasting related to acute and chronic disease (*anorexia-cachexia syndrome)* (Morley *et al.*, 2006; Rolland *et al.*, 2006).
3. Anorexia in the elderly may be also related to *environmental factors* (income, cooking facilities, retirement/leisure time, education, distance to food store, availability of transportation, social activity, self-esteem, symbolism of food, mental awareness).
4. *Iatrogenic conditions* (side effects of drugs, hospitalization).

It is, however, difficult to verify the real cause of anorexia (different causes may coexist) and this may influence the prevalence, in different settings, of anorexia of ageing (Horwitz *et al.*, 2002).

3.3.2 Epidemiology

From an epidemiological point of view, nutritional surveys show a low to moderate prevalence of frank nutrient deficiencies in free living elderly groups. The SENECA-EURONUT study, enrolling cognitively intact and free living elderly from twelve European nations, found that dietary intakes were often below the recommended levels established for younger adults but this was not reflected in the indicators of nutritional status (del Pozo *et al.*, 2003). The National Health and Nutrition Examination Survey has clearly shown a linear decline in food intake from 20 to 80 years in both men and women, even if this change could be caused by a greater incidence of pathological causes in elderly

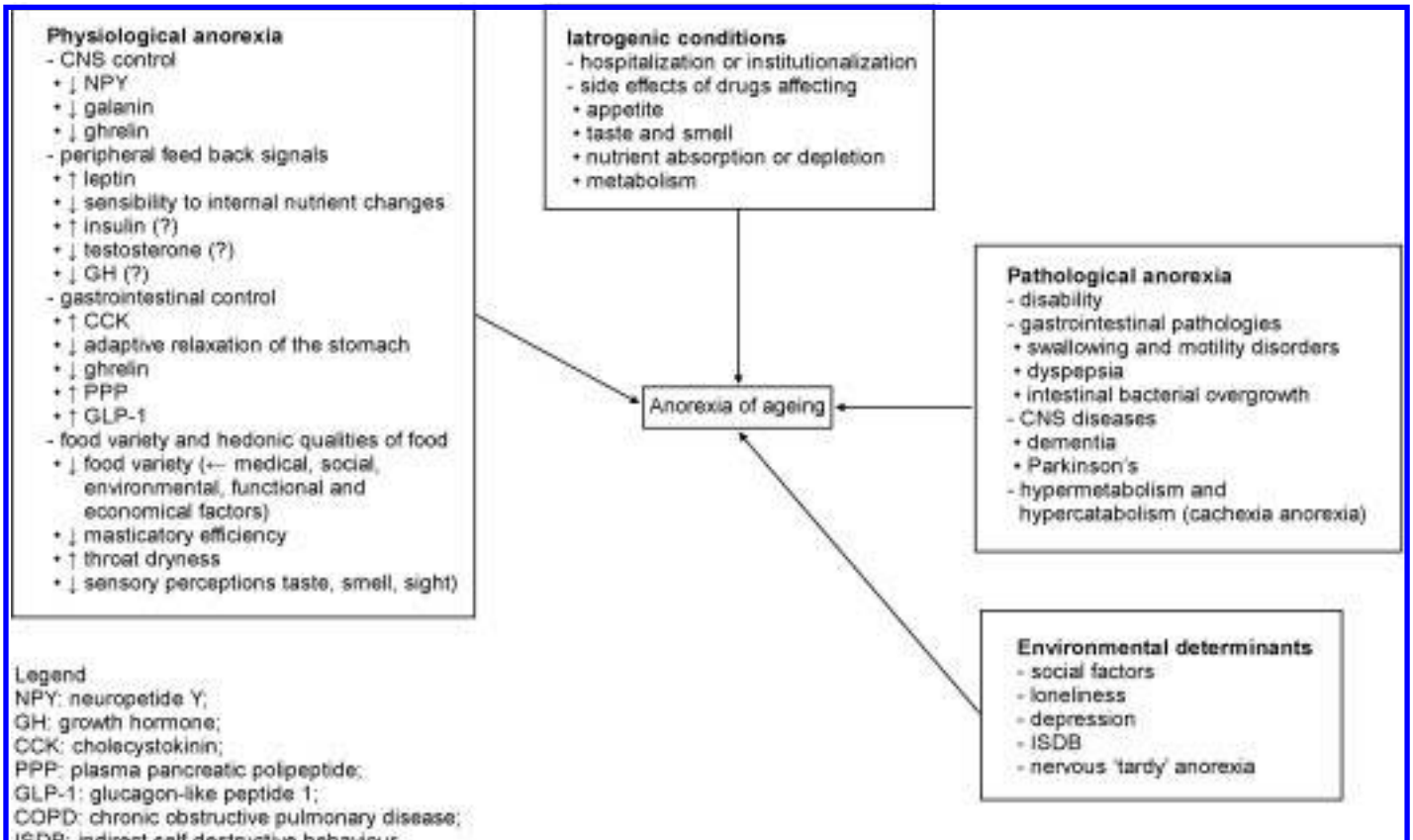

Fig. 3.2 Anorexia of ageing.

people (Anon., 1994). In another study the authors found that food intake was lower in older persons than in younger: their data showed that the major decrease was due to a decrease in fat (55%) rather than in carbohydrate (40%) intake (Sullivan, 1995). The macronutrient composition appears, however, to vary considerably both within and between populations (De Groot *et al.*, 2000).

According to different records of cases and nutritional parameters, data are worst in institutionalized older persons whose rates of protein energy malnutrition range from 30 to 60% (Kagansky *et al.*, 2005; Westergren *et al.*, 2002; Shum *et al.*, 2005). In particular in these populations, *sarcopenia* characterized by a loss of muscle mass and muscle strength, plays a main role in the development of frailty, resulting in functional and metabolic impairments and physical disabilities. It leads to increased morbidity, mortality, and a number of hospitalizations with extended stays (Sullivan, 1995; Marzetti & Leeuwenburgh, 2006).

3.3.3 Pathogenesis (Fig. 3.2)

Physiological anorexia of ageing

Energy balance and food intake regulation control mechanisms in the elderly are altered as different studies underline. In fact, healthy older persons ingest less energy than younger men do during a single meal. However, when given a preload (e.g., yoghurt) the elderly fail to adequately regulate their food intake, overeating 10–30%, whereas younger adults had a more precise regulation of their food intake (Elia *et al.*, 2000; Henry, 2000).

Healthy elders have also been shown to be less hungry at meal initiation and to become more rapidly satiated during a standard meal compared to younger adults. Other studies in healthy elderly individuals have shown that men who consume diets over several weeks, providing either too few or too many calories relative to dietary energy needs, subsequently do not compensate for the resulting energy deficit or surplus when provided an *ad libitum* diet (Hays & Roberts, 2006; Roberts, 2000). For this reason older individuals are considered less capable of returning to their previous weight after a perturbation of their food intake than the younger are and even after refeeding, older persons return to a lower weight than previously.

These findings are consistent with the suggestion that a lack of the normal ability to regulate energy intake contributes to impaired energy regulation in old age. However, rather than consider this as an independent factor, the reduction in the ability to regulate food intake should be placed in the context of an overall reduction in the ability to deal with adverse events (Roberts, 2000).

Central nervous system control on food intake

Decreased concentrations of endogenous opioid peptides and of their effectiveness, related to the opioid receptors reduction, occurs with ageing. Elderly patients with idiopathic senile anorexia seem to have lower levels of cerebrospinal fluid and plasma β-endorphin. Even NPY is less effective in increasing

food intake in older than in younger animals and its concentration declines with ageing especially in Alzheimer's dementia patients. Intracerebroventricular administration of orexin A and NPY stimulated food intake in young and adult rats, but no effects were observed at any dose in old rats. Data on orexin contribution to anorexia of ageing are not definite while it seems that there is an increase of central activity of CART mediated by the normal age-related decline in testosterone (Chapman, 2004).

Galanin circulating levels do not differ between young and old women after correction for body fat, but reduced sensitivity may contribute to senile anorexia (Chapman, 2004).

One possible explanation for altered metabolism during ageing is reduced ghrelin/GHS-R signalling caused by lower production of ghrelin. Some authors (Rigamonti *et al.*, 2002; Sturm *et al.*, 2003) found that plasma ghrelin values in old subjects of normal weight were markedly lower than in young adults of normal weight. It has been shown that ghrelin increases food intake in a dose-dependent manner, and the effect of ghrelin is reduced with advancing age. Neither the acylated nor the desacyl plasma ghrelin level differed significantly between young and old rats (Akimoto-Takano *et al.*, 2005).

The lower ghrelin levels in the old subjects were accompanied by increased insulin levels and low serum IGF-I. The former was a predicted compensatory mechanism for age-related insulin resistance, and the latter is consistent with age-dependent hyposomatotropism rather than malnutrition. In undernourished subjects the data are not conclusive: some authors (Sturm *et al.*, 2003) found that plasma ghrelin concentrations (total active ghrelin and inactive desoctanoyl-ghrelin) were higher in undernourished older than in the well-nourished older and young subjects, while in other studies this observation is not confirmed. Moreover, ghrelin activity seems to be reduced in older subjects (not only undernourished) because of ghrelin resistance and/or increased ratio of desoctanoylated ghrelin/ghrelin.

According to some authors, an increased ratio of tryptophan (a serotonin precursor) to large neutral amino acids has been found in the cerebrospinal fluid of patients with idiopathic senile anorexia (Martinez *et al.*, 1993).

The issue concerning the production of interleukin with anorexic action (IL6, TNFα) in geriatric age is disputable. Studies in this field, up to now, did not give any unequivocal result; some of them showed an increased production of IL6 also without any chronic or acute illness in course, while others did not reach similar conclusions (MacIntosh *et al.*, 2001b; Beharka *et al.*, 2001; Yeh *et al.*, 2001).

Peripheral feedback signals

Decline in food intake in the elderly may be due to altered regulation of peripheral feedback signals such as those coming from fat cells. In healthy elderly, anorexigenic signals prevail over orexigenic signals, and they contribute to prolonged satiety (in particular, postprandial satiety) and inhibition of hunger. Fasting leptin is normally higher in the elderly than in the young and

postprandial fluctuations are not significant. Fasting insulin also is significantly higher in the elderly than in the young and the postprandial insulin rise is greater in the elderly (Di Francesco *et al.*, 2006).

Leptin levels increase with adiposity and age, and remain elevated above levels of young animals even after a 72 h fast. This may be related to age-related failure of the network of hypothalamic neurons to appropriately integrate hormonal and neural inputs, or to a failure of the neurons to produce the appropriate neuropeptides (Hays & Roberts, 2006). In a recent paper the authors hypothesize that sequential, age-related alterations in the expression patterns of neuropeptides that maintain melanocortinergic tone, and in the hormone mediators that inform the system of the state of energy balance, result in a diminished ability to maintain energy homeostasis with increasing age (Wolden-Hanson, 2006).

In animal models, leptin administration selectively decreases visceral fat and inhibits hepatic glucose production Therefore, the relationship between the age-related increase in visceral fat and increased insulin resistance may involve the failure of centrally acting leptin to regulate fat distribution. Moreover aged rats are less responsive to leptin because of impaired regulation (by fasting or leptin infusion) of hypothalamic NPY synthesis (Wang *et al.*, 2001; Scarpace *et al.*, 2000).

Several studies in humans have demonstrated that, after adjustment for body fat, a significant inverse relationship between serum leptin and age exists. However leptin concentrations are not dramatically altered with ageing and seem to be more related to body fat than ageing per se, leaving open the possibility that disrupted leptin signals, as opposed to increased leptin levels, occur in age-related energy imbalance such as anorexia (Chapman, 2004).

Peripheral feedback signals may come also from the rate of peripheral nutrient utilization and the plasma nutrient concentrations that influence circulating messages relating to overall fuel status. Changes in regulatory systems occurring in the elderly may cause difficulties in maintaining metabolic and nutritional homeostasis. Ageing is associated also with a decline in the sensitivity to both internal and environmental changes. Circulating glucose is thought to be one of the signals of hunger in younger adults and detection of hypoglycaemia may be impaired in older individuals. With ageing, glucose may still be an important mediator of changes in the regulation of food intake even if its impairment is not quantitatively important.

In the same way available evidence suggests an increase in circulating fatty acid concentrations with normal ageing in humans, particularly in association with increased fat stores and inactivity. This increase may therefore contribute to the increase in circulating CCK concentrations and decreased appetite (Parker & Chapman, 2004).

Also circulating hormones may influence food intake. Insulin has been suggested to act as a satiety agent by affecting the expression of neuropeptides (such as NPY) and insulin concentrations increase with ageing as a result of increased insulin resistance. At the moment, there are no data supporting the role

of insulin in the development of the anorexia of ageing. Nevertheless animal studies have reported that hyperglycaemias and or hyperinsulinemia may be causes of the greater satiating effects of glucose in older subjects (Chapman, 2004; Beharka *et al.*, 2001).

Sexual hormones are well recognized to regulate appetite: testosterone increases food intake. Thus the reduction of its levels in older males may play a role in the reduction of food intake (reduced ghrelin, increased CART and leptin levels) and in the loss of muscle mass, too (sarcopenia) (Morley, 2001a,b; Roberts, 2000; MacIntosh *et al.*, 2001a).

GH may have independent effects on appetite and food intake. Production and circulating concentrations of GH decline in the elderly, contributing to the body composition changes that accompany ageing. Although little is known about GH effect in humans, clinical observations suggest that GH treatment may increase food intake in children with growth disorders and muscle mass in malnourished elderly subjects (Parker & Chapman, 2004).

Gastrointestinal control on food intake

In the elderly, more rapidly acting or more potent inhibitory satiety signals may contribute to the altered regulation of the satiation system. Nutrients passing into the small intestine and their absorption contribute to stimulate the release of hormones. These include cholecystokinin (CCK), glucagon-like peptide-1, glucose-dependent insulinotropic peptide, insulin and amylin, all of them with proven or putative satiating effects.

CCK is probably the most important satiating hormone and is thought to be responsible for 20% of the signals responsible for meal termination. Animal studies have shown greater levels and an increased satiating effect of CCK in older compared with younger animals (Chapman, 2004). Many authors found that elderly patients with idiopathic senile anorexia had increased plasma concentrations of CCK compared with age-matched controls (Chapman *et al.*, 2002).

Satiation system regulation is under the control of the adaptive relaxation of the stomach fundus. With ageing, food tends to transit more rapidly from the fundus into the antrum and then to remain longer there, leading to earlier and greater degree of antral relaxation. This is directly proportional to the development of satiation after ingestion of a meal. The reduction of the number of neurons in the myenteric plexus and the decrease of nitric oxide are associated with diminished adaptive relaxation of the fundus stomach in the elderly. Even if the condition may not be the same in humans, in studies with older animals there is a reduction in messenger RNA for NO-synthase with ageing (MacIntosh *et al.*, 2001a,b).

Elderly frequently complain of increased fullness and early satiation during a meal and many studies have reported a decreased rate of gastric emptying in the elderly. This may precede antral distension and therefore represent a potential important factor underlying the differences in hunger perception and satiation between young and older subjects. In fact, in a recent paper (Sturm *et al.*, 2004)

it was found that antral area and (presumably) antral distension are related to satiation and satiety. Moreover, delayed gastric emptying presumably prolongs the period during which energy substrates remain in the circulation and this substrate availability has been postulated as a central mediator of food intake regulation (Hays & Roberts, 2006).

Circulating ghrelin levels decline during ageing probably because of impaired function of the gastric mucosa. Indeed, the membrane thickness, the glands length and the endocrine cells number in the gastric mucosa decrease in animals between puberty and old age (Hays & Roberts, 2006; Khomerki, 1986; Sandstrom *et al.*, 1999; Smith *et al.*, 1997). However, how peripheral and central components of ghrelin action are functionally interrelated are still to be discovered. Chronic treatment of elderly subjects with ghrelin mimetics restores the age-related decline in amplitude of GH pulsatility and circulating IGF-1 to levels typical of young adults (Chapman *et al.*, 1996a,b). These results suggest that during ageing either ghrelin production declines or ghrelin resistance occurs. The orexigenic property of ghrelin coupled with its anabolic effects via the GH/IGF-1 axis and its inhibition of the production of inflammatory cytokines (Dixit *et al.*, 2004) indicate that rescue of reduced GHS-R activity by treatment with exogenous ghrelin or ghrelin mimetics may be beneficial in the anorexia of ageing.

Ghrelin increases feeding mainly in young, fast growing animals. However, in older animals, peripheral ghrelin improved feeding when injected repeatedly over several days. At least under these conditions, ghrelin effect is mediated by the AP/NTS region. Using repeated administration, ghrelin might be an interesting tool to increase feeding in patients suffering from wasting diseases such as cancer anorexia (Gilg & Lutz, 2006; Neary *et al.*, 2004).

Ageing is associated with decreased growth hormone (GH) secretion, appetite and energy intake. As ghrelin stimulates both GH secretion and appetite, reductions in ghrelin levels may be involved in the reductions in GH secretion and appetite observed in the elderly. Plasma levels of acylated ghrelin, in particular in elderly female subjects, positively correlate with serum IGF-I levels and bowel movement frequency and negatively with systolic blood pressure (Hays & Roberts, 2006; Akamizu *et al.*, 2006).

In a recent paper the authors found that, plasma pancreatic polypeptide concentrations show a marked diurnal rhythm. Basal and postprandial pancreatic polypeptide concentrations increase with age. The much higher pancreatic polypeptide concentrations in older people will induce increased satiety that may contribute to anorexia of ageing (Johns *et al.*, 2006).

Glucagon and GLP-1 also may contribute to anorexia of ageing: its levels seem to be elevated in the elderly and many evidences suggest a role in the enhanced satiation associated with old age (Hays & Roberts, 2006).

Food variety and hedonic qualities of food

In some studies (Hsu-Hage & Wahlqvist, 1996; Fanelli & Stevenhagen, 1985) the authors found that as subjects got older, they were more likely to have lower

food variety. A decline in the variety of food choices and consumption of a nutritionally inadequate diet is likely to be the result of a combination of medical, social, environmental, functional, and economic factors that influence eating habits and nutritional status of elderly people (Bernstein *et al.*, 2002). Dietary variety has been shown to decline as age increases, with sensory impairment, poverty, loneliness and widowhood. Elderly food choice is oriented to: make shopping easier (stocking of great quantity of foods versus variety, precooked food), facilitate meal preparation (cooking a lot of foods which are stocked in the fridge and consumed after being warmed up, exposing the elderly to reduced intake of vitamins), facilitate ingestion (soft, easy to chew foods which do not exacerbate oral pain during chewing and swallowing). These and other age-related situations can potentially interfere with food intake and emphasize the need for diverse food choices to promote adequate nutritional intake. Dietary variety is in fact associated with several biochemical measures of nutritional status (Hsu-Hage & Wahlqvist, 1996; Bernstein *et al.*, 2002).

The enjoyment of food is related to taste but also to smell as it approaches the mouth, and the release of volatile organic substances within the mouth also contributes to the enjoyment of food. In addition food temperature and texture, as well as masticatory sounds, all produce the ultimate sensory experience.

A progressive atrophy of the salivary glands, the lack of nutrients (Zn), drugs use (such as diuretics, anticholinergic drugs, drugs for treatment of Parkinson's disease, tricyclic antidepressants) may cause throat dryness in elderly with important consequences for food intake.

Poor dentition or ill-fitting dentures may be considered a factor affecting elderly nutrition and even masticatory efficiency of removable dentures is much less than that of complete natural dentition. Partial or total edentulism affects the quality of life and the health status since it deeply limits the hedonistic component of feeding and thus food selection. In fact, the elderly, even wearing dentures, tend to avoid specific foods such as those of hard, fibrous texture, as meat, fruits (such as, for example, apples, pears) and vegetables (such as, for example, raw carrots, raw fennels) in order to reduce or eliminate oral pain. Thus a softer texture is therefore the main changed organoleptic characteristic used as coping behaviour. In fact, by means of this behaviour, the elderly do not reduce total energy intake since selected foods are generally rich in simple sugar, saturated fats and cholesterol and are even able to cause overweight or obesity in those with oral disease. However this behaviour is characterized by a reduction of the intake of animal proteins, vitamins and minerals and may frequently cause malnutrition. According to most studies, a functionally inadequate dental status affects nutritional status and, although some differences are present in different studies, daily intake of non-starch polysaccharides, protein, calcium, non-haem iron, niacin, vitamin C and intrinsic and milk sugars are generally significantly lower in edentate. Consequently nutritional parameters (albumin and haemoglobin, plasma levels of ascorbate and retinol) tends to be lower for edentulous elderly subjects (Sheiham & Steele, 2001; Soini *et al.*, 2005; Krall *et al.*, 1998; Sahypun *et al.*, 2003).

Masticatory efficiency may also be negatively affected by drugs like muscle relaxants or benzodiazepines, by serious illnesses compromising: motility (Parkinson's disease, cerebrovascular disease, major depression), musculature efficiency, generally speaking (myasthenia, hypothyroid myopathia) or that regarding the mouth in particular (oculo-pharingeal muscular distrophy, cerebrovascular accident) (De Groot *et al.*, 2000; Haller *et al.*, 1996a). Ageing is characterized by a reduction in *sensory perceptions*: visus sharpness decreases, olfactory and gustative thresholds increases, hearing and tactile discriminative capacity decreases (Hays & Roberts, 2006). These changes negatively affect the hedonistic features of all the steps of feeding.

As mentioned before, taste and smell are key determinants of food palatability. Poor appetite, inappropriate food choices and consequently lower nutrient intake may occur with advancing age and are mainly related to chemosensory losses.

In the elderly taste thresholds increase because of the reduction of taste papillae: in particular sweet taste is less affected than other modalities (sour, salt, bitter) and salt shows the highest increase. Similarly, older persons are less able to identify different compounds. Taste dysfunction may also result from certain diseases, medications, surgical interventions, malnutrition and environmental exposure, bad oral hygiene or when a dental prosthesis is used.

The ability to smell declines progressively with age in relation to diseases or medications, while older persons rate flavour as the most important determinant of their food choice. With ageing, threshold reductions have been reported for multiple odorants and many disorders affecting smell perception like anosmia, hyposmia and dysosmia increase in severity with advancing age. Some authors (Doty *et al.*, 1984; Elsner, 2001) found that older persons preferred food having a greater flavour concentration. Addition of simulated food flavours to meats, vegetables and other foods to amplify smells to compensate for chemosensory losses has been shown to be helpful in an elderly population resulting in an improved immunity and functional status, palatability and food acceptance.

Sight is basic for eating behaviour. By sight it is possible to evaluate: shape, dimension, appearance, and colour of foods. Colour plays a very important role in food choice, since it allows assessment of food appearance, it arouses expectations of taste, odour, texture, healthiness; it also provides signs about maintenance of food. In food choice or rejection sight is the first control point working in parallel with experiences and memories. In fact, people are reticent when tasting differently coloured food and this fact suggests that food choice or rejection is made up by a complex evaluation based on both sensory perceptions and memories (Schiffman & Graham, 2000; Mulligan *et al.*, 2002).

Pathological anorexia of ageing

Disease usually appears differently in a person over 65 years old than it would in a younger adult or child. Decrease in appetite may be, for example, a symptom of worsening of heart failure, as well as early onset of pneumonia, or alterations in gastrointestinal status (Amella, 2004).

Despite being apparently healthy, most of the elderly suffer from one or more chronic conditions, which may produce anorexia, malabsorption and increased metabolism, alone or in combination. Decline in food intake in the elderly may be due to different medical conditions:

- *Disability*: even if little information exists on the association of disabilities and macronutrient intakes, limitations in daily life activities are considered a key cause of weight loss.
- *Gastrointestinal pathologies*: swallowing and motility disorders are associated with aspiration and decreased food intake; dyspepsia is extremely common in older persons and is associated with anorexia; persons with intestinal bacterial overgrowth have been shown to lose weight associated with both anorexia and malabsorption; *helicobacter pylori* infection prevalence increases with age and may play a role in anorexia.
- *CNS diseases*: in elderly patients affected by Alzheimer's dementia it is still unclear whether weight loss precedes or follows dementia and whether it is caused by low levels of energy intake or by a hypermetabolic state. In people affected by dementia the control of feeding intake (deregulation of the central opioid feeding drive, CCK increase, reduced levels of plasma and brain NPY and brain norepinephrine, changes in sensorial perception) seems to be affected. Moreover problems concerning deterioration of mental status (loss of memory of the latest meal, apraxia of eating, agnosia with difficulties in interpreting sense data related to vision, taste, smell or touch, distraction from eating during mealtime) may contribute to difficulties in eating. Even changes in behavioural function (circadian shift in intake preponderance of calories consumed at breakfast) and the loss of the Activities of Daily Living (inability to buy food, to cook meals, to feed themselves and feeding time lengthening) may create a serious risk as far as nutrition is concerned (Reynish *et al.*, 2001; Young & Greenwood, 2001). Patients with Parkinson's disease often exhibit eating problems: most of them show a decreased sense of smell, a cognitive decline, a loss of motivation to eat related to depression, difficulties in starting to eat owing to increased need for external stimulation or in performing the acts of eating. Moreover Parkinson's disease drugs may cause anorexia and further contribute to decreasing food intake (Cushing *et al.*, 2002; Fiske & Hyland, 2000).
- *Hypermetabolism and hypercatabolism* (cachexia-anorexia): the release of cytokines increases energy and protein requirements and produces anorectic and wasting effects. The anorectic effect of cytokines (IL1, IL-6 and TNF-α) is mediated by: leptin (release and action on leptin receptor), direct stimulus of corticotrophin- releasing-factor, increase of $PGE_{1\alpha}$ levels, inhibition of orexigen peptides release (dynorphin, NPY, galanin). Other factors may, however, be present and contribute to anorexia. Up to half of patients suffering from femoral neck fracture have a malnutrition (sarcopenia in particular) with consequences on quality of life, difficulties in recovery from functional impairment. In this case, malnutrition is related not only to

anorectic cytokines increased production, but also to difficulties in purchasing food and in preparing meals and to inadequate food choice (Carlsson *et al.*, 2005). Moreover, in chronic obstructive pulmonary disease (COPD) anorexia may be secondary to increased metabolism, due to increased activity of the respiratory muscles, but also to oxygen desaturation and to experiences in meal-related situations. In a recent study, findings showed consistency between COPD, nutritional status and descriptions of eating difficulties, feelings of dependence, level of activity, transport of food, having company or being alone, appetite, hunger and need of time were correlated with nutritional status (Odencrants *et al.*, 2005).

Many medical conditions may also affect the sense of taste and smell and thus food intake (Chrischilles *et al.*, 1992; Carr-Lopez & Phillips, 1996; Schiffman, 1993). These conditions are:

- those affecting the nervous system (Alzheimer's disease, epilepsy, multiple sclerosis, Parkinson's disease)
- those concerning the nutritional sphere (chronic renal failure, cancer, zinc – vitamin B12 – niacin deficiencies) – endocrine diseases (diabetes mellitus, hypothyroidism) – local inflammations (allergic rhinitis, bronchial asthma, sinusitis) – and viral infections (acute viral hepatitis, influenza-like infections).

Environmental and psychological causes of anorexia

One of the causes of anorexia of ageing is the loss of motivation to eat that may be due to depression and loss or deterioration of social networks (Hays & Roberts, 2006).

Social factors, like poverty, inability to shop, to feed oneself, to prepare and cook meals, can contribute to decreased food intake in the elderly (de Castro & de Castro, 1989; Thompson & Morris, 1991; Morley & Kraenzle, 1994, 1995). Moreover, few people achieve healthy nutrition daily and constantly. The concept of a healthy diet is not so unanimously shared and older subjects often have false beliefs about it, leading them to monotonous eating habits (Hughes *et al.*, 2004).

Less energy is acquired during meals consumed alone than during meals eaten with others (de Castro, 1993, 1994). Appetite and nutrient intake may be improved by an extensive friendship network while loneliness and widowhood may cause a decrease in meal enjoyment, poorer appetite and weight loss. However, providing food via specific social programmes may not overcome the eating problems associated with social isolation. Such data are generally used to suggest that social eating promotes overeating and obesity, but another interpretation is that eating alone, in the elderly especially, leads to under-nourishment and weight loss.

Depression has been shown to be one of the most important treatable causes of weight loss in both community and institutional settings. Depression is related to loneliness, low self-esteem, intolerance against the environment, retirement from

job, loss of a relative or a pet, hospitalization or retirement in a nursing home (McIntosh *et al.*, 1989; Rosenbloom & Whittington, 1993). The mechanism behind anorexia in depression has not been fully elucidated. There is some evidence that depression increases corticotrophin releasing factor (CRF) levels, suggesting a role for CRF causing anorexia and weight loss in the elderly. The prevalence of depression is high in the elderly. Geriatric Depression Scale (GDS) scores above the cut-off of 5 were found in about 12% of the men and 28% of the women enrolled in the SENECA study. There was a significant negative correlation between GDS score and cholesterol blood levels. Successful treatment of depression in nursing home residents results in reversal of weight loss. Weight loss and anorexia were found to be important symptoms related to increased mortality in depressed elderly (Haller *et al.*, 1996b; Pulska *et al.*, 2000).

Refusal to eat can be part of an indirect self-destructive behaviour (ISDB) a form of covert, indirect and perhaps unconscious suicidal behaviour. ISDB is defined as an act of omission or commission that causes self-harm that leads indirectly and over time to the patient's death. Persons can omit behaviours that would sustain life and health like prescribed treatments or food. ISDB has been shown to be associated with a direct suicidal potential, dissatisfaction with the treatment programme and life in general, confused reasoning and judgement, poor prognosis for discharge, absence of religious commitment and significant losses in the patient's life. Some older people decrease their food intake a few months before dying: for those patients who feel an excessive burden of life, refusing food is an acceptable method for terminating their lives (Marcus & Berry, 1998).

Nervous or 'tardy' anorexia can recur in older persons who were previously weight restrictors. Eating disorders have been considered illnesses of adolescence and young adulthood but few cases of later onset (over 50 years of age) presentation have been reported in literature. These patients have a persistently depressive mood but a lesser degree of disturbed body image and of preoccupation with weight, eating and shape (Pulska *et al.*, 2000; McIntosh & Hubbard, 1988).

Iatrogenic anorexia

Hospitalization or institutionalization in a nursing home, independently from physical acute illness, forecasts a reduction of feeding intake; all this leads to worsening of mood, to the perception of a likely future loss of the family environment, besides the loss of all of those non-biological values nevertheless attributed to food intake. The foods we eat as well as when, where and how we eat them are decisions based on individual choices and lifetime habits. In a nursing home or in a hospital these choices are limited. Therefore, many elderly refuse to eat because they do not like the food they are served or because the food is of different ethnicity. In a recent survey, only 23% of the residents in a nursing home were very satisfied with the food and 58% stated choice and control over food to be very important. Nursing home residents or hospital patients may also reject food to punish a staff member who has not been kind to

them, as a way to manipulate the staff itself, to get more attention or to refuse a dietary prescription (Kane *et al.*, 1997; FSCP, 2002).

Side effects of drugs: comprising 12% of the population, elderly persons consume 35% of prescription drugs in the United States. Epidemiological studies indicate that the mean number of medications used by community-dwelling elderly over the age of 65 ranges from 2.9 to 3.7 medications (Morley, 1997). The side effects of these drugs are a major cause of weight loss in older persons both free living or institutionalized. Drugs can affect nutritional intake by:

- decreasing appetite: digoxin, amiodarone, spironolactone, cimetidine, amitriptyiline, most antibiotics, metronidazole, amantadine
- causing malabsorption, nausea or vomiting: sorbitol, theophyllin elixir, laxatives
- increasing metabolism: excess thyroxine replacement, theophylline
- depleting the body's mineral stores: aluminium or magnesium hydroxide antacids, diuretics.

In addition, drug-induced depression, cognitive impairment and constipation may cause food refusal (Carlsson *et al.*, 2005; Odencrants *et al.*, 2005; Marcus & Berry, 1998; Kane *et al.*, 1997; Alibhai *et al.*, 2005).

Over 250 medications (Carlsson *et al.*, 2005; Odencrants *et al.*, 2005) have been clinically reported to alter taste and/or smell like drugs:

- to lower cholesterol or lipids in blood: fibrates, statines
- antihistamines
- to fight infectious diseases: antibiotics, fluoroquinolones
- to treat cancer
- for arthritis and pain: corticosteroids
- for asthma and breathing problems: β-adrenergic agonists
- for hypertension: ACE inhibitors, Ca-channel-blockers
- for heart disease: nitroglycerin patches
- muscle relaxants
- for Parkinson's disease or epilepsy treatment
- to improve mood.

Compared to young individuals, the average detection thresholds for elderly individuals, with one or more medical conditions and taking an average of 3.4 medications, were 11.6 times higher for sodium salts, 4.3 times higher for acids, 7.0 times higher for bitter compounds, 2.7 times higher for sweeteners (Schiffman & Graham, 2000; Chrischilles *et al.*, 1992).

3.4 Conclusions

In the elderly an adequate food intake can contribute to improved well-being and quality of life. Further studies are necessary to better understand factors contributing to poor nutrition in the elderly, such as changes in various

neurotransmitters, and to develop preventive (reduction of risk factors, improvement of nutritional assessment) and treatment strategies (nucleotides, increased energy and nutrient density food, improving taste and smell).

Dietary interventions in older adults should aim to prevent decline and to extend possible restoration of function and quality of life. Interventions need to be acceptable, integrated with other health-promoting strategies and continually monitored to evaluate their effectiveness.

It is very important to keep in consideration and face anorexia of ageing in due time (Carr-Lopez & Phillips, 1996). Consequences of malnutrition, as stated, can be extremely serious and deeply affect patients' morbidity, mortality and quality of life. Therefore, it will be of the utmost importance to:

- insert a special evaluation of the nutritional risk in the Comprehensive Geriatric Assessment, that must be performed in all elderly patients at admission, and evaluate the nutritional status and food intake of older patients using specific and validated tools (Eating Behaviour Scale (Tully *et al.*, 1997), Blandford Scale (Blandford *et al.*, 1998), Mini Nutritional Assessment (Guigoz *et al.*, 1994)
- identify and treat, when possible, the disease (acute and chronic infections, depression) underlying anorexia
- institute environmental and behavioural modifications (change in atmosphere during mealtime, providing favourite foods, increasing food flavours, seeking companionship during meals, increasing physical activity)
- improve staff knowledge and organisation to produce higher quality feeding assistance during mealtimes (Simmons *et al.*, 2001)
- use, in selected cases, appetite stimulants (megestrol acetate, cyproheptadine, growth hormone)
- plan early nutrition rehabilitation programmes (liquid supplements, enteral feeding (Wilson *et al.*, 2002)) and nutritional education programmes for caregivers (enabling them to establish a minimal evaluation of the nutritional state, to know the nutritional value of basic food, to cope with eating behaviour disorders (Morley, 2001b; Pulska *et al.*, 2000; Riviere *et al.*, 1998, 2001; Thomas *et al.*, 2000)).

3.5 Sources of further information and advice

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4

Sensory perception of food and ageing

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Abstract: Sensory perception of food is complex and involves, apart from non-chemical skin senses, vision, audition and kinesthesis, the chemosensory modalities of olfaction, gustation and chemesthesis which underlie flavour perception. This chapter describes the functions of the chemical senses and the role they play for food intake, it reviews age-related changes in chemosensory perception and their possible causes, and presents possible consequences of these chemosensory changes for food intake and well-being in the elderly population.

Key words: olfaction, gustation, kinesthesis, flavour, ageing.

4.1 Introduction

Studies show that 3–10% of non-institutionalized elderly and 25–60% of institutionalized elderly suffer from malnutrition (Swedish National Food Administration, 1998; Vellas *et al.*, 2001). Health-related consequences of the anorexia of ageing are extensive and well-documented, and together with other psychological, social, and medical factors, age-related changes in sensory perception are likely to contribute to these problems (MacIntosh *et al.*, 2000). Sensory perception of food is complex and involves the sensory modalities of olfaction, gustation, chemical and non-chemical skin senses, vision, audition and kinesthesis to provide the individual with information about the food's flavour, temperature, colour, appearance, and texture.

Apart from presbyopia (poor accommodation due to inflexibility of the lens) which is a normal ageing process in vision, macular degeneration, diabetic retinopathy, cataract and glaucoma are relatively common ocular conditions among elderly people that result in reduced visual acuity and contrast sensitivity, loss of visual field, scotomas, glare sensitivity as well as image and colour

distortion (Whiteside *et al.*, 2006). Regarding audition, in addition to the normal ageing process of presbyacusis (sensorineural loss), conductive loss and central hearing loss are fairly common causes of hearing difficulties in the elderly population (Wallhagen *et al.*, 2006). Ageing also takes its toll on non-chemical skin senses of importance for food perception, such as touch and temperature (Wickremaratchi and Llewelyn, 2006). However, the most important sensory systems for food perception are the chemical senses that provide information about flavour, the senses of olfaction, gustation and chemesthesis. The relevance of these senses in this context is illustrated by the fact that flavour is ranked by elderly consumers as the most important determinant for food purchase (Krondl *et al.*, 1982; Madeira and Goldman, 1988).

The objectives of this chapter are to (i) provide a description of the functions of the chemical senses and the role they play for food intake, (ii) review documented age-related changes in chemosensory perception and their possible causes, and (iii) present possible consequences of these chemosensory changes for food intake and well-being in the elderly population.

4.2 Function and general role of the chemical senses

From an evolutionary perspective, the chemical senses of olfaction, gustation, and chemesthesis are very old sensory systems, and therefore differ considerably in function and role from younger senses such as vision and audition. The following section provides a brief description of the chemical senses and their integration.

4.2.1 Olfaction

Odorous molecules reach the olfactory epithelium, located in the roof of the nasal cavity, through the orthonasal passage, which is enhanced by sniffing. However, important for food perception, the molecules can also reach the epithelium from the oral cavity through the retronasal passage, which is enhanced by movements of the tongue, cheek and throat that pump the molecules through this passage (Burdach and Doty, 1987). The olfactory epithelium contains the olfactory neurons with their olfactory receptors located on cilia that are embedded in the olfactory mucus. The receptors have specifically shaped proteins to which the odorous molecules can bind and activate the olfactory neurons, after having penetrated the mucus (Moon and Ronnett, 2003). The neurons project through the cribiform plate to the olfactory bulb where they make contact with mitral cells (and interneurons) over a gap of synaptic connection. The mitral cells, in turn, project to higher-order olfactory areas, including the pyriform cortex, orbitofrontal cortex, amygdala and enthorinal cortex (Zald and Pardo, 2000).

The human capacity to discriminate odour qualities is particularly good; possibly tens of thousands of qualities can be distinguished, made possible by as

many as 250 to 750 genes that code for olfactory receptors, of which about half are pseudo genes (Buck and Axel, 1991; Ressler *et al.*, 1994). Each gene determines the shape of a certain receptor type, which, in turn, determines the type of odorous molecule that can bind to the receptor. Each neuron only expresses one receptor type (Strotmann *et al.*, 1992). However, importantly for quality discrimination, most odorous substances consist of hundreds of molecules (Laing *et al.*, 1989), and all olfactory neurons with a particular receptor type project to the same group of neurons in the olfactory bulb. Thus, when an odorous substance consisting of several different molecules is presented, a predetermined activity pattern is generated in the olfactory bulb that is characteristic for that particular odorous substance. This pattern is then interpreted by areas at higher levels of the olfactory system enabling, for example, recognition and identification.

The most important function of human olfaction is to guide our attention towards hazards (e.g., spoiled food and poisonous fumes) and towards items that in a general sense have positive connotations (e.g., nutritious food). With a few possible exceptions, there appears to be no innate preference for odours. Instead, a prerequisite for an odorous substance to warn or attract us is that we at an earlier encounter with the substance associate its odour with a positive or negative emotion depending on the context, and that we at the later occasion recognize the odour and retrieve the association from memory (Engen, 1991). The relatively strong emotions often evoked by odours are believed to enhance the appropriate behavioural response. Not surprisingly, once encoded in memory, the forgetting curve for odour recognition is over time rather flat (Engen and Ross, 1973). Neuroanatomical support for this notion is provided by the fact that the amygdala is an area of general importance for memory encoding and emotional experience and expression as well as for primary processing of olfactory information (Zald and Pardo, 1997; Aggleton and Young, 2000), and that the primary olfactory cortex (piriform and enthorinal cortices) has strong neural links to the hippocampal formation of particular importance for recognition. The hedonic dimension is the dominating aspect of odour perception (Richardson and Zucco, 1989). The pleasantness/unpleasantness of an odorous item, such as food, is to a large extent determined by an individual's personal history with that item. Hence, the hedonic aspect is easily emotionally conditioned.

4.2.2 Gustation

Taste cells are found in groups of 30 to 50 in the membranes of taste buds. A pore at the top of the taste bud makes contact with the outside fluid environment in the mouth, and the taste molecules bind to taste receptors in the taste cell's hair-like cilia at the pore. The taste cells make contact with primary taste nerves over a gap of synaptic connection, and project to higher brain regions. The taste buds are contained in groups in three types of structures called papillae that are visible to the eye: fungiform (distributed over the anterior 2/3 of the tongue), foliate (along the posterolateral margins of the tongue) and circumvallate

papillae (extended in a V-shaped line across the root of the tongue; Witt *et al.*, 2003). Three cranial nerves innervate the taste system: VII innervates the fungiform papillae of the anterior tongue (chorda tympani branch) and taste buds on the palate (greater superficial petrosal branch); IX (glossopharyngal) innervates the foliate papillae on the rear edges of the tongue, and the circumvallate papillae on the back of the tongue; and X (vagus) innervates receptors in the throat (Duffy and Bartoshuk, 1996). Sweet, salty, sour and bitter tastants innervate all cranial nerves (Bartoshuk, 1993) and can be perceived on any area of the tongue (Nordin *et al.*, 2007). The taste information is carried by the cranial nerves to the solitary tract in the medulla, and from there to the ventroposteromedial thalamic nucleus, and further to the anterior insula (primary taste cortex). Other important brain areas involved in taste processing include the orbitofrontal cortex and amygdala (Rolls and Scott, 2003).

Bartoshuk and colleagues (e.g., Bartoshuk *et al.*, 1994) have devoted considerable effort to the issue of individual differences in taste sensitivity due to genetic variation. These differences in sensitivity have been found for certain bitter compounds, such as caffeine, phenylthiocarbamide and 6-n-propylthiouracil. Based on detection thresholds, individuals can be categorized as 'tasters' (sensitive) and 'non-tasters' (relatively insensitive); about a thousand-fold higher threshold concentration compared to 'tasters').

The gustatory system functions as a final gatekeeper of the internal milieu, acting to guide ingestive and avoidance behaviours (Smith and Scott, 2003). As in odour perception, hedonic value is an important perceptual dimension of taste perception, with close ties to motivational behaviour. It is likely that the traditional taste qualities subserve signalling functions about the presence of nutrients or dangers: carbohydrate energy sources in sweetness and sodium in saltiness, whereas sour and bitter warn for danger from acids and toxins, respectively. As a consequence, humans are born liking sweet and disliking bitter and sour (Lawless, 1985). Apart from the four basic taste qualities, a fifth quality, called umami ('delicious taste' in Japanese), is today recognized as an additional basic quality by a large number of scientists in the field. Its sensation can be referred to as 'brothy', 'savoury' or 'meaty', and is evoked by monosodium glutamate.

4.2.3 Chemesthesis

Chemesthesis refers to chemosomatosensory function (also called the common chemical sense) that is activated by chemical substances that stimulate open nerve endings, so-called nociceptors, located in the nasal cavity, oral cavity and cornea. The neural signals are transmitted to the brain via the three branches of the trigeminal nerve. The sensations can be characterized as stinging (e.g., carbon dioxide in soda), burning (e.g., chilli pepper), cooling (e.g., peppermint), or astringent (e.g., wine). Practically all substances can evoke one of these sensations if the substance reaches a sufficiently high concentration (Doty *et al.*, 1978), and can at high concentrations generate pain.

The primary function of the intranasal chemesthetic system is to act as a sentinel of the airways where it reflexively stops inspiration to prevent inhalation of potentially life-threatening substances (Silver, 1991). Thus, it is to an even larger extent than olfaction a chemical warning system since substances with strong activation are likely to be potentially harmful. The warning feature is further illustrated by defence reflexes in the body in response to this type of chemical stimulation, such as sweating, tearing and salivary flow.

4.2.4 Flavour

Olfactory, gustatory and chemesthetic perception are closely integrated (Cain and Murphy, 1980; Lawless and Stevens, 1984), and as a consequence difficult for the individual to separate when perceived simultaneously. The blended perception of these sensory systems in response to food in the oral cavity constitutes flavour, which is dominated by odour perception (Rozin, 1982). This perceptual unity can be explained by its neuroanatomy with cortical neurons that are specialized for this integration. There are, for example, neurons in the orbitofrontal cortex and insula that are activated only when odorants and tastants are presented simultaneously (Rolls and Baylis, 1994; Francis *et al.*, 1999).

4.3 Chemosensory perception and food intake

Regulation of energy balance is controlled by metabolic mechanisms and meal behaviour, both being influenced by chemosensory function. This influence can be referred to the onset of the meal, its continuation and its termination with consequences for when and how much we decide to eat. The chemical senses do also shape human eating behaviour in terms of what we decide to eat.

4.3.1 When to eat

Mechanisms that enhance the onset of the meal and that prepare the individual for the meal include food cravings and hunger, which are both emotional in character and motivate food intake. The food cravings reflect to a large extent cravings for specific chemical stimulation to satisfy somatic needs for nutrients and minerals. A craving of such kind is positive alliesthesia. Alliesthesia can be both positive and negative in character and described as a change in food pleasantness (palatability) caused by internal chemical signals from the food (e.g., glucose in the intestines; Cabanac, 1971). In positive alliesthesia the flavour of a specific nutrient that the body is deficient of is perceived as particularly pleasant (Fig. 4.1). Examples include the very pleasant taste of sweetness when the blood-glucose level is low, and the very pleasant taste of saltiness when the body's need of additional salt is large, resulting in increased likelihood of ingesting these substances.

In addition to the chemical senses' influence on intake of food that we at the

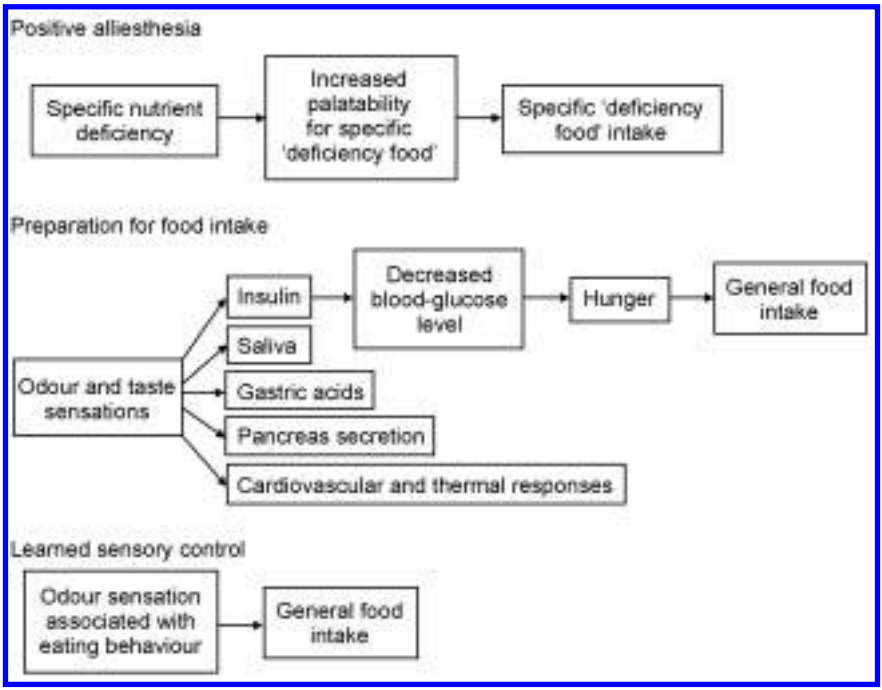

Fig. 4.1 Mechanisms involving the chemical senses that enhance the onset of the meal and prepare the individual for the meal.

moment are in specific need of, the smell, taste, sight and even thought of food, encourage general food intake. This is accomplished by both biological and psychological mechanisms. The biological mechanisms prepare the individual for the meal by stimulation from the food sensations to, for example, secrete insulin (Fig. 4.1). The insulin will lower the blood-glucose level and generate a sensation of hunger to start general food intake. Odour and taste sensations from food do also improve the metabolism of nutritions, carbohydrates and fats by triggering a number of reflexes. These include secretion of saliva, gastric acids and substances from the pancreas as well as cardiovascular and thermal responses (Richardson *et al.*, 1977). An important psychological mechanism is so-called learned sensory control, in which food cravings are evoked by classical conditioning of the food sensations that have been associated with the behaviour to start eating (Fig. 4.1).

4.3.2 How much to eat

During a meal, two groups of sensory mechanisms oppose each other: one group that enhances continued eating, and another group that enhances termination of eating. The difference in strength between these two groups determines to a large extent the size of the meal (Davis and Levine, 1977). The former group includes smell and taste sensations that stimulate dopaminergic and serotonergic

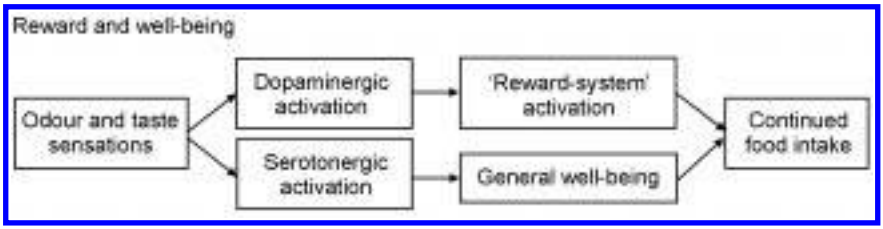

Fig. 4.2 Mechanisms involving the chemical senses that enhance continued eating.

systems in the CNS (Fig. 4.2). Dopaminergic activation stimulates the 'reward system', whereas serotonergic activation evokes general well-being, encouraging continued eating (Neill and Cooper, 1988). The orbitofrontal cortex, insula and amygdala are important regions for emotional 'reward' and 'punishment' for food intake, with consequences for motivation and food behaviour (Francis *et al.*, 1999; Rolls, 2000). Opioids play an important role in this respect by acting directly on the amygdala, but also on the hypothalamus, to enhance appetite and food intake (Levine *et al.*, 1985).

The chemical senses' role in termination of the meal includes negative alliesthesia, sensory-specific satiety and learned sensory control. The two first mechanisms affect the individual's relation to specific foods, and the third mechanism affects the relation to food in general. Negative alliesthesia implies, contrary to positive alliesthesia, that the pleasantness of 'superfluous' food fades as more of this specific food is consumed (Fig. 4.3). This mechanism is activated by signals from the digestive system, in particular by uptake of glucose in the blood and by increased concentration of nutrients in the intestines

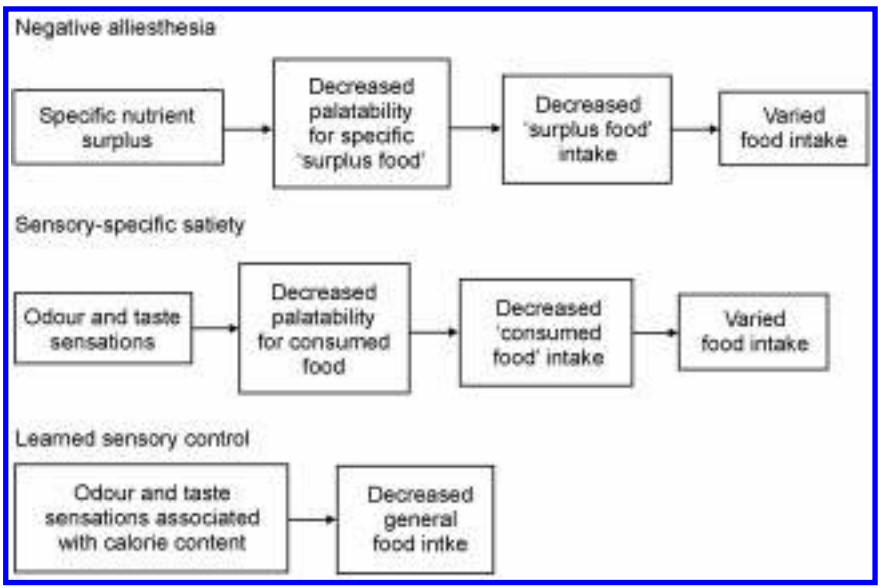

Fig. 4.3 Mechanisms involving the chemical senses that enhance termination of eating.

(Cabanac and LeFrance, 1990). This encourages consumption of a variety of different foods.

In sensory-specific satiety a relatively large intake of food with the same flavour leads to decreased sensory appreciation for this particular food, more than for food with other flavours (Fig. 4.3). Although sensory-specific satiety, as negative alliesthesia, results in faded palatability, these two phenomena differ in an important aspect: alliesthesia is generated by somatic signals, whereas sensory-specific satiety is generated by external, sensory signals. Sensory-specific satiety is not directed towards food in general, but to food with sensory properties similar to the food that has been consumed (Rolls *et al.*, 1981). As for negative alliesthesia, this encourages intake of different foods.

The importance of the chemical senses in sensory-specific satiety is demonstrated by findings suggesting that the satiety is not dependent on food reaching the stomach. The specific role of olfaction in this respect is illustrated by both perceptual and neurophysiological data. In accordance with decreased pleasantness in flavour, the odour pleasantness decreases with increased satiety for the type of food consumed, but less so for other foods (Rolls and Rolls, 1997). It has also been shown that activity in the orbitofrontal cortex in response to exposure of food odour is affected by the satiety in a specific manner; the neurons that will show most prominent decline in activity depends on the food odour that has been consumed to satiety (Critchley and Rolls, 1996). Taste and visual sensations do also contribute to sensory-specific satiety (Rolls *et al.*, 1982).

In addition to preparing the individual for a meal, learned sensory control does also contribute to the termination of the meal (Fig. 4.3). Birch and Deysher (1985) had preschool children eat snacks with high- and low-calorie content at different occasions. The two types of snacks were flavoured differently to enable associations between flavour and calorie content. The results showed that the children learned to predict calorie content based on the flavour and that they adjusted the meal size depending on the flavour.

4.3.3 What to eat

Food preference and aversions strongly affect what we decide to eat, and are to a large extent influenced by prior experiences by means of classical and instrumental conditioning. In this respect the chemical senses, olfaction in particular, play important roles due to their ability to easily make strong associations (Baeyens *et al.*, 1988). We learn very early in life, primarily based on olfactory cues, how to identify an item with respect to its edibility (Schaal *et al.*, 1998). Preferences are formed throughout life, and begin even before birth by flavours in the amniotic fluid from the mother's food intake (Mennella and Beauchamp, 1993; Mennella *et al.*, 1995). Regarding food aversions, signals from the sense of smell to area postrema in the brainstem evoke nausea and vomiting that underlie aversions. Olfactory associations, followed by gustatory, appear to be the most common reason for food aversions (Nordin *et al.*, 2004).

4.4 Age-related changes in chemosensory perception

Changes in chemosensory function can be both quantitative and qualitative in nature. Quantitative changes include detection sensitivity, intensity discrimination and perceived intensity, whereas quality changes refer to quality discrimination. A review will follow that describes age-related impairment in chemosensory perception and their possible causes.

4.4.1 Olfaction

A vast number of studies have demonstrated substantial impairment in various olfactory functions in elderly persons when presenting food and non-food odorants orthonasally. The decline in function includes detection sensitivity (Schiffman *et al.*, 1976; Schiffman and Pasternak, 1979; Stevens and Cain, 1987; Stevens *et al.*, 1987; Cain and Gent, 1991; Hummel *et al.*, 1997) and quality discrimination (Schiffman, 1977: Schiffman and Pasternack, 1979; Schiffman and Leffingwell, 1981; Stevens and Lawless, 1981; Hummel *et al.*, 1997; Kaneda *et al.*, 2000). It seems that an age-related loss in detection sensitivity for one odour quality is accompanied by a loss in detection of other qualities (Cain and Stevens, 1989; Cain and Gent, 1991). Although very weakly perceived intensities will compromise discrimination, studies of neuroimaging, calcium imaging and psychophysics suggest largely independent, parallel processing of odour intensity and quality discrimination (Cain *et al.*, 2008; Rawson *et al.*, 1998; Savic *et al.*, 2000).

Diminished perceived odour intensity has also been suggested in the older population (Stevens and Cain, 1985, 1987; Wysocki and Gilbert, 1989), and Stevens and colleagues (1989) have demonstrated stronger olfactory adaptation and slower recovery in the elderly population. Importantly, loss in olfactory sensitivity does not appear to be inevitable to each ageing individual. Thus, in studying a group of successfully aged elderly who were carefully screened for medical and lifestyle factors known to affect olfaction, Almqvist and collaborators (1992) obtained detection thresholds that were very similar to thresholds for young adults.

For general evaluation of the sense of smell, in both clinical and non-clinical settings, it is common to assess the ability to identify (name) odorous items. This ability requires intact detection sensitivity (assumed to underlie relatively strong odour sensation), quality discrimination, and recognition memory, which all are important olfactory functions for human daily routines (Hummel and Nordin, 2005). As would be expected based on the given review, studies show clear impairment in odour identification in the elderly (Schiffman, 1977; Schemper *et al.*, 1981; Doty *et al.*, 1984; Murphy, 1985; Stevens and Cain, 1987; Wysocki and Gilbert, 1989; Ship and Weiffenbach, 1993; Cain *et al.*, 1995; Duffy *et al.*, 1995; Hummel *et al.*, 1997; Larsson *et al.*, 2004). Results from population-based studies show that prevalence rates for olfactory dysfunction, by means of tests of cued odour identification, increase from 11–24% in middle-aged individuals to 37–70% at the age of 70 years (Murphy *et al.*, 2002; Brämerson *et al.*, 2004).

Age-related decline in other cognitive functions of olfaction are also well documented (e.g., Larsson, 1997).

Olfactory dysfunction in older adults has also been found with respect to physiological processing of odour stimuli presented orthonasally. Recordings of electrophysiological cortical activity by means of olfactory event-related potentials (ERPs) suggest that neuronal allocation (reflected by the amplitudes) is diminished and that processing speed (reflected by the latencies) is decreased in normal ageing for both relatively sensory and cognitive components of the ERP (Murphy *et al.*, 1994; Evans *et al.*, 1995; Hummel *et al.*, 1998; Morgan *et al.*, 1999; Murphy *et al.*, 2000). Neuroimaging with fMRI suggests age-related decrease in activity in the enthorinal cortex, piriform cortex, amygdala and periamygloid cortex, hippocampus and parahippocampal gyrus, orbitofrontal cortex and insula when conducting tasks requiring low-cognitive olfactory functioning (Cerf-Ducastel and Murphy, 2003; Wang *et al.*, 2005).

Elderly have to some extent also been investigated regarding retronasal olfaction. In accordance with orthonasal stimulation, impairment has been found with respect to detection and quality discrimination (Cain *et al.* 1990; Stevens and Cain, 1993; Duffy *et al.*, 1999), perceived intensity (Stevens and Cain, 1986a), and identification (Murphy, 1985).

4.4.2 Gustation

Taste dysfunction is in general much less common than smell dysfunction (Goodspeed *et al.*, 1987; Deems *et al.*, 1991). The robustness of this sense may be explained by the fact that as many as three cranial nerves innervate the taste system. It is therefore not surprising that age-related impairment is also less prominent for taste than for smell (Weiffenbach, 1984; Cain *et al.* 1990). Nevertheless, decline in gustatory function is often present in the ageing individual. Elevated taste-detection thresholds in elderly compared to young adults is a common finding (Grzegorczuk *et al.*, 1979; Schiffman *et al.*, 1979; Weiffenbach *et al.*, 1982; Murphy *et al.*, 1995), and the slope describing taste intensity as a function of tastant concentration has been shown to be flatter for elderly than for young (Schiffman and Clark, 1980; Weiffenbach *et al.*, 1986). It is of interest to note that significantly poorer taste sensitivity has been reported in institutionalized elderly in comparison to non-institutionalized (Spitzer, 1988). It has also been demonstrated that elderly are poorer in detecting the presence of salt (Stevens *et al.*, 1991) and marjoram (Cain *et al.*, 1990) in soup.

Old persons do also seem to have poorer ability than the young to discriminate tastants with respect to both intensity (Gilmore and Murphy, 1989; Nordin *et al.*, 2003) and quality (Kaneda *et al.*, 2000), and they perceive food and non-food taste stimuli as weaker (Stevens and Lawless, 1981; Murphy and Gilmore, 1989), and are poorer in identifying basic taste qualities (Nordin *et al.*, 2007).

Importantly, there seems to be quality-specific age-related changes in taste perception when reviewing studies of changes in detection sensitivity, intensity discrimination and perceived intensity in which sensitivity to two or more basic

taste qualities have been assessed in the same individuals (Hyde and Feller, 1981; Hyde *et al.*, 1981; Weiffenbach *et al.*, 1982, 1986; Bartoshuk *et al.*, 1986; Enns and Hornung, 1988; Gilmore and Murphy, 1989; Murphy and Gilmore, 1989; Kaneda *et al.*, 2000; Nordin *et al.*, 2003). Although the results are not fully consistent, bitter sensitivity seems to be most affected by age, and sweet sensitivity least affected, whereas salty and sour sensitivity fall in between.

4.4.3 Chemesthesis

Although age-related effects have been studied considerably less regarding chemesthesis compared to olfaction and gustation, data suggest that ageing takes its toll also on this chemical sense. Using predominantly CO_2 as a trigeminal intranasal stimulus, but also other stimuli with irritating properties, results from investigations suggest poorer detection sensitivity in elderly than in young adults. This has been demonstrated when expressing detection sensitivity as the traditional threshold and the reflex apnea threshold (Murphy, 1983; Stevens and Cain, 1986b; Shusterman *et al.*, 2003), and as the trigeminal lateralization threshold (Hummel *et al.*, 2003; Wysocki *et al.*, 2003). In line with these threshold data, ageing does also appear to suppress perceived intensity of irritating stimuli (Stevens *et al.*, 1982; Murphy, 1983). Laska (2001) compared young and elderly in their ability to discriminate between chemical stimuli with trigeminal properties, and found a modest decline with age.

Further support for age-related effects on chemesthesis is provided by electrophysiological data. Compared to young adults, elderly have been shown to require a stronger concentration to elicit a negative mucosal potential which reflects activation of the nociceptors in the nasal cavity (Frasnelli and Hummel, 2003). Hummel and associates (1998) have also demonstrated smaller chemosomatosensory ERP amplitudes in elderly than in young adults.

4.4.4 Pleasantness and preference

Pleasantness mediated by sensory characteristics of food is a strong determinant of food choice (Clark, 1998). Loss in chemosensory sensitivity is therefore likely to affect pleasantness and preferred concentration of food components, since intensity is a powerful predictor of hedonic tone. Indeed, diminished perception of saltiness and sweetness in the elderly has been reported to lead to increased pleasantness and preference for these tastants (Murphy and Withee, 1986; Zallen *et al.*, 1990; Drewnowski, 1997). Murphy and Withee (1987) did also show that elderly people, particularly those with low nutritional blood values, perceive amino acids (common food flavours) in an amino-acid-deficient soup base as less strong than did young participants, and preferred higher concentrations. Furthermore, de Graaf and associates (1994) reported that elderly, on average, perceive high concentrations of food flavours to be less intense than do younger adults, and that optimal pleasantness concentrations of the flavours are higher in the elderly. The authors also suggested that olfaction contributed more than gustation to this age-related effect on flavour perception.

4.4.5 Causes of age-related changes in chemosensory perception

Possible causes of the age-related alterations in olfaction reviewed above include neuroanatomical changes in olfactory receptor cells, bulb, and tract, entorhinal cortex, hippocampus, and amygdala (Liss and Gomez, 1958; Scheibel and Scheibel, 1975; Tomlinson and Henderson, 1976; Price *et al.*, 1991). Owing to very early and extensive neuropathology in both peripheral and central olfactory areas, patients with Alzheimer's disease are likely to constitute a special risk group regarding olfactory impairment and its consequences for food perception. Thus, this population shows severely impaired sensory- and memory-based olfactory functions (Nordin and Murphy, 2002). Impaired olfactory function is also common in other neurodegenerative diseases, such as Parkinson's (Mesholam *et al.*, 1998) and Huntington's (Nordin *et al.*, 1995a) diseases.

Neuroanatomical degeneration is also likely, at least partly, to explain the age-related changes in taste perception. Thus, ageing is typically accompanied by reduction in receptor-cell, taste-bud, and papilla density (Arey *et al.*, 1935; Miller, 1989). An interesting finding regarding odour discrimination's relative independence of odour detection in elderly (Cain *et al.*, 2008) is that receptor cells collected in biopsies from humans and studied for responsiveness to odorants via calcium imaging have shown broader tuning for older than for younger subjects (Rawson *et al.*, 1998). However, less is known about age-related changes in the gustatory CNS.

A large number of medical conditions are known to affect olfaction and gustation, and old persons are susceptible to the same causes of chemosensory dysfunction as are all age groups, as well as to causes more specific to ageing (Seiberling and Conley, 2004). The most common etiologies of olfactory disorders among patients seeking medical attention at ENT clinics include upper respiratory infection, chronic sinusitis, nasal polyposis, allergic rhinitis, and head trauma (Nordin *et al.*, 1996: Temmel *et al.*, 2002; Brämerson *et al.*, 2007). Common etiologies of gustatory disorders are head trauma and upper respiratory infection (Bartoshuk and Duffy, 1995).

Adults over 65 years of age take in on average 2.9 to 3.7 medications, and institutionalized elderly take about twice as many (Finkelstein and Schiffman, 1999). It has been suggested that more than 250 drugs may alter smell and taste sensations. These include antihistamines, lipid-lowering drugs, antimicrobial medications, antineoplastic medications, asthma medications, antihypertensives, muscle relaxants and antidepressants (Schiffman, 1991). Nutritional deficits, such as reduced levels of zinc and vitamin A and B, are known to affect smell and taste sensitivity and hedonics (Friedman and Mattes, 1991; Schiffman, 1997). The effects of malnutrition on chemosensory perception may, in turn, affect food intake and aggravate the state of malnutrition.

Poor oral health in elderly, such as tooth loss, may affect taste and retronasal smell perception (Ship, 1999; Seiberling and Conley, 2004), and dentures has been suggested to increase the risk of impaired flavour perception (Duffy *et al.*, 1999). Saliva is important for taste function by carrying sapid molecules to the receptors and by containing substances capable of modulating taste responses.

Although salivary function appears to be relatively unimpaired in healthy ageing, dry mouth is a common complaint among elderly who take medication (Bradley and Beidler, 2003).

4.5 Consequences of age-related chemosensory changes for food intake and health

Patients with olfactory loss commonly complain about diminished quality of life, affected interpersonal relations, worry about not perceiving toxic substances and possible poor personal hygiene, difficulties with daily routines, and depression. The loss of chemosensory sensations which constitute the primary reinforcers of eating in these patients often result in poor food appreciation and decreased appetite, with change in body weight as a consequence. These patients also report difficulties preparing food and they worry about eating spoiled food (Hummel and Nordin, 2005).

It is therefore not surprising that data from elderly with changes in olfactory and gustatory perception suggest accompanied poor food appreciation and appetite, change in food choice such as decreased dietary variation, poor nutritional status, change in body weight and increased risk for chronic disease (Brown, 1976; Stevens and Lawless, 1981; Krondl *et al.*, 1982; Fanelli and Stevenhagen, 1985; Mattis-Kulig and Henkin, 1985; Ferris and Duffy, 1989; Wysocki and Pelchat, 1993; Mattes and Cowart, 1994; Duffy *et al.*, 1995; Griep *et al.*, 1995; Morley, 2001). Rolls and McDermott (1991) have demonstrated that elderly do not show as strong sensory-specific satiety as young adults, which may explain the decreased dietary variation with age. However, not all studies have shown a relation between chemosensory impairment and nutritional problems (Ferris and Duffy, 1989), and lack of sensory feedback from eating, may in some cases actually lead the individual to eat more and become obese.

Certain aged subgroups are likely to constitute particular risk groups due to age-related chemosensory loss. For example, the effect of age-related changes in saltiness and sweet perception on food choice may have considerable consequences for elderly with hypertension and diabetes (Murphy, 1992). Since diminished taste perception appears to lead to increased preference for relatively strong concentrations of the tastant (Murphy and Withee, 1986; Zallen *et al.*, 1990; Drewnowski, 1997), it becomes difficult for these individuals to adhere to a low-salt and low-sugar diet.

There is a considerable risk among elderly to ingest spoiled food. It has, for example, been suggest that elderly adults are less likely than young adults to reject foods with unpleasant odours (Pelchat, 2000). Probably due to the very gradual decline in olfactory function, elderly individuals in general, and patients with Alzheimer's disease in particular, are commonly not aware of their loss in olfactory sensitivity (Nordin *et al.*, 1995b). The unawareness aggravates the risk of ingesting spoiled food, since these persons are less likely to take precautions to avoid eating spoiled food. It can be assumed that the risk among elderly in

general of ingesting spoiled food is also increased due to the age-related impairments in bitter-taste sensitivity and chemesthesis.

The impact of age-related changes in chemosensory perception on food intake, nutritional status and health is an important issue for the gerontological field to deal with. Schiffman and her research group have obtained very important and encouraging results that show that anorexia in the elderly often remits when foods are amplified by additional flavouring (e.g., artificial chicken flavour on a chicken dish) to compensate for diminished chemosensory function (Schiffman and Warwick, 1988). More specifically, results from her research suggest that additional flavouring will increase institutionalized elderly persons' preference for and intake of food (Schiffman, 1998), increase salivation (Schiffman, 1998; Schiffman and Miletic, 1999), and improve immunological status and grip strength (Schiffman and Warwick, 1993).

4.6 Future trends

As reviewed above, it is well documented that the chemical senses influence when, how much and what the human individual ingests. A considerable volume of research has also been conducted over the past decades to investigate perceptual, neuroanatomical and neurophysiological changes in olfaction and gustation in normal and pathological ageing. From this research it is clear that various aspects of the sense of smell are impaired in the ageing individual. Although the gustatory system may be less affected by the ageing process than the olfactory, taste function can also be considered to decline with age. However, there is yet very limited knowledge of age-related pathological changes in the gustatory CNS that can account for the perceptual changes. However, valid procedures that apply fMRI to study brain activity in relation to taste perception are today available and may well enable a fruitful future research area to help fill this knowledge gap. A related question to be approached is the relative degree to which the alterations in the chemical senses are caused by normal ageing processes or rather by diseases, medications, cognitive status or environmental factors.

Despite the vast number of studies that have been conducted on age-related alterations in chemosensory perception, there are certain issues that deserve further attention. This includes the question of age-related quality-specific loss in taste function, which has implications for certain subgroups with specific needs to adhere to a restricted diet of nutrients or minerals, but also with implications for food safety and for general food intake in the normal ageing population. The conclusion that sensitivity to bitter taste is most impaired in elderly, sweet taste being least impaired, and salty and sour taste being moderately impaired is still somewhat premature and calls for further study. Research in chemesthesis has grown rapidly in the past decade, with a rather large number of laboratories today focusing on this sensory system. The need for further understanding of perceptual and neural chemesthetic changes in ageing

and its consequences for food intake is therefore likely to be met within the near future.

Another important issue that has received intensified attention and is likely to become a future research trend is the linkage between age-related chemosensory changes and general health in the ageing population. Findings of an association between age-related changes in chemosensory perception and poor food appreciation and appetite, change in food choice, poor nutritional status, change in body weight and increased risk for chronic disease shows the importance to further consider the chemical senses to enable adequate food intake and health in the ageing population. However, existing data on this issue are almost exclusively obtained from studies with cross-sectional designs. Thus, longitudinal studies should be conducted for satisfactory understanding of the cause-effect mechanism.

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5

The social significance of older people's meals

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If any member of the family should be absent, the empty place at table is a mute reminder of the missing person; when the children have all grown up and left home, the parents, left behind, face each other across the expanse of the table, which after twenty years or more … is haunted by memories of the dramas that have certainly taken place round this symbol of the family itself

(Visser, 1991: 82)

Abstract: Old age and isolation has been recognized as a dilemma and especially eating alone. One problem with loneliness, besides being deprived of human contact, is the effect it has on nutritional status. In this chapter the phenomenon of sharing food and eating together is discussed from different perspectives both among free living older persons and among elderly living in institutions. It is pointed out that commensality is the end of a long process involving food as an indication of social occasions and that a close social network is a determining factor for eating and household work. Also being able to care for oneself and being able to shop for and cook food and prepare meals are part of older people's personhood. Though eating alone not necessarily entails malnutrition it is mostly associated with less enjoyment in eating. It is also discussed that it is important to recognize the social and cultural implications of food and meals when examining commensality as a phenomenon.

Key words: older, food, meals, social networks, commensality, culture.

5.1 Introduction

Food is, as Maslow points out, the most important necessity for human survival (Maslow, 1970). But food is more than nutrition and fuel, as has been stressed by anthropologists and sociologists in numerous research papers published over the years (e.g., Douglas, 1972; Levi-Strauss, 1969; Mennell *et al.*, 1992). In people's everyday lives, the meaning of food is illustrated by the way we choose food, shop for food, talk about food, cook, eat and behave at table. The cultural and social significance of food and meals is, therefore, strongly connected to our identity as human beings and as members of society. There are some scholars, such as Yoder, who have suggested that all daily activities that are food related in some way or another are connected to people's lives (Berg *et al.*, 2003). Because food is a natural part of human life, it becomes part of the meaning of life. In other words, planning, procuring, preparing, presenting and consuming food becomes part of the expression of everyday human life. Consequently, when everyday food-related activities are drastically changed, the expression of identity and the self through food will also be altered.

Growing old in modern society is associated with problems, but also with a positive attitude implying that ageing is not worth worrying about and can be postponed (Torres and Hammarström, 2006). Compared to the past, older people today are more likely to cope by themselves in everyday life and thus be more independent (Tinker, 1997). Life expectancy has increased, and old people live longer, healthier lives. Recently, attitudes towards embodied old age have been more positive than earlier theories in gerontological discourses have shown, which may be explained by the consumer culture we all belong to (Öberg and Tornstam, 2003). However, the ageing process will inevitably cause problems for the ageing population as they grow into advanced old age (Torres and Hammarström, 2006). The older one becomes, the more likely isolation will be recognized as a dilemma (Tinker, 1997). As could perhaps be expected and as has now been documented in a longitudinal study, the increase in loneliness is highest for those reaching the oldest ages (Dykstra *et al.*, 2005). The increase in loneliness is not the same for all older adults; single-living people can be less lonely than those living with a partner. However, those whose partner has died show the greatest increase in loneliness. Changing family structures, in which children no longer live close to their old parents, old friends become sick or die, and the development of the impersonal urban environment are the causes of this dilemma.

However, the notion that conditions were more favourable in the past, when three generations lived in the same household, is considered a myth by some scholars (Tinker, 1997; Fennell *et al.*, 1988). In contemporary society, in contrast to the past, old people are more likely to have a great deal of contact with their grandchildren. Yet, according to Perren *et al.* (2004), there is no evidence that older people aged 80 and above develop relationships or can count on receiving help from neighbours, which may reflect a lack of social contact. However, in a study by Nocon and Pearson (2000), there are examples of friends

and neighbours giving old frail people support in everyday life. A study by Perren *et al.* (2004) suggests that older men are more likely to have frequent conversations with neighbours than are older women. However, concerning neighbourly exchange, older men who are living alone are less likely to receive or give favours than are those living with others, while the reverse is true for older women. One problem with loneliness, besides being deprived of human contact, is the effect it has on nutritional status. A study by Walker and Beauchene (1991) showed that, among older persons age 60–94 years, loneliness and social isolation were related to dietary inadequacies. In a recent study by Locher *et al.* (2005), it was revealed that ethnicity and gender were risk factors for older people's nutritional intake. Old black women were most at risk, followed by old black men and old white women. The researchers concluded that what contributes most to nutritional risk is social isolation, low income level, limited support and social capital, including limited transportation to food shops and congregated meal sites, as well as a limited independent life-span (Locher *et al.*, 2005).

5.1.1 Eating together

Sharing food and eating together constitute a symbol of community, of holding the group together and of strengthening the group. George Simmel claimed that eating together was a prerequisite of democracy (Simmel, 1910). From a gender perspective, one of the most dominant features of living in partnerships is the sharing of food and a meal (Kemmer *et al.*, 1998). Commensality, which means sharing food or sharing the table, is the end of a long process involving food as an indication of social occasions. Planning, preparing, cooking and serving food are steps on the way to sharing food as a meal with family members, relatives and friends. Thus, cooking is just as much a social occasion as the sharing of a meal. Food, and especially meals, are consequently often associated with the construction and cementation of family ties (Valentine, 1999; Charles, 1990/1995; DeVault, 1991). The family is, thus, the most established and most symbolically idealized commensal unit (Sobal, 2000).

In a study by McKie *et al.* (2000), people over 75 years of age and living in Scotland were interviewed about their beliefs on food and health. One of the results presented was that healthy eating was equivalent to eating 'proper meals'. This by now well-known concept, first highlighted by Charles and Kerr (see Charles, 1995) and Murcott (1995) during the 1980s, means eating a cooked dinner involving traditional foods. In McKie *et al.*'s (2000) study, a proper meal also connotes a family event, which implies a social event. According to the interviews presented in the Scottish study, the older generation was brought up on proper meals. In a more recent European study entitled 'Food in Later Life' (FiLL), in which older persons aged 65 to over 90 and from eight European countries were interviewed about food in everyday life, this was also clear in the memories of the older men and women who participated (Mattsson Sydner *et al.*, 2007). The close social network, which for most of the informants was the

traditional nuclear family, had been a determining factor for diet, eating and household work throughout their life. Margaret Visser suggests that, not long ago, the ultimate gesture of intimacy was to invite strangers to share a meal in the kitchen, because this room symbolized a space that was essentially only for the family (Visser 1991). Thus, food habits are not a question of individual choice, but a matter of close social relationships, including planning, buying, preparing, cooking and serving a meal.

5.1.2 Eating alone

The desire for close connects, as articulated by Tinker (1997), reflects a fundamental human need. Sharing a meal, coming together in commensality, would thus also be a human need, and one effect of isolation is not being able to share meals with other people. In a study on senior citizens in Florida, USA, it was shown that older persons participating in a senior nutrition programme that provided nutritious meals to county residents reduced their social isolation and improved their health (Smith *et al.*, 1994). In contrast, it was shown in another study in the US that meal programmes, with Meals-on-Wheels, can both improve nutritional intake and maintain nutritional risk for vulnerable seniors (Keller, 2006). Thus, eating alone could be interpreted as a risk for malnutrition. Nevertheless, in studies examining dietary intake in older women and men who are living alone or cohabiting, differences in energy intake have not been seen (Andersson, 2002; Shahar *et al.*, 2001). On the other hand, older people who were living alone, especially those who had lost a spouse, and in particular women, reported that they ate more meals alone and felt less enjoyment in eating (Shahar *et al.*, 2001; Sidenvall *et al.*, 2000; Wylie *et al.*, 1999; Quandt *et al.*, 1997).

We can, however, expect, that changed food-related routines, meals and social relations in everyday life will or may have long-term negative effects, if not on older people's nutritional status, at least on their feeling of well-being and quality of life, which is an outcome as undesirable as malnutrition. Shahar *et al.* (2001) found that widowhood had effects on all food-related work, including shopping, cooking and eating, which resulted in weight loss. In addition, Martin *et al.* (2006) found that eating alone, social isolation and stressors were the main reasons older people gave for their low weight. Yet in a study by Pollina and McKee (2000), the opposite was found: eating alone could cause overweight and other nutritional problems among older women 51–91 years of age. Most studies on meals and eating have been conducted on older women. However, in a study by Hughes *et al.* (2004), older men who were living alone and 62–94 years of age were interviewed about food and meals in everyday life. Most men believed they had adequate cooking skills or were good cooks, although their vegetable and fruit intake did not meet nutritional requirements. Nevertheless, their life satisfaction was good. Compared to what has been reported about older women, older men seem to have a more positive relationship to food, which may explain their contentment with food in everyday life.

In a recently published psychological study in the UK, it was observed that eating alone was the situation that caused people to eat the least amount of food (Hetherington *et al.*, 2006). Sharing a meal with family, or familiar others, increased energy intake by 18 percent compared to baseline (eating alone); however, eating together with strangers did not result in a specific increase in food intake. The situation that gave the next highest increase in food intake was when the subjects were watching TV. During meal situations in front of the TV, food intake increased by 14 percent compared to baseline. For the general population, eating while watching TV should perhaps not be recommended, considering the risk of obesity. However, for older people who feel lonely and are at risk for loss of appetite that would result in weight loss, watching TV while eating could be good companionship and thus it would be positive. When older Swedish women who were living alone talked about wanting to share a meal with someone but having to eat alone, they reported that the TV provided good company during a meal (Sidenvall *et al.*, 2000). However, these women did not consider it proper to eat in front of the TV! In their narratives, they declared that you should sit at the table while eating a meal, whether you were alone or not. Thus, normative beliefs such as this should perhaps be called into question.

5.2 The dependent older person

The notions of dependency and independency inevitably arise when discussing old age (Fenell *et al.*, 1988; Tinker, 1997; Hockey and James, 1993). Being independent and taking care of oneself are important aspects of older people's health and well-being (Shiu, 2001; Berg *et al.*, 2006). Taking care of food and meals in everyday life is, therefore, an essential part of people's well-being (Gustafsson *et al.*, 2003). In an interview study conducted in Norway with older hospitalized persons, it was shown that health was a matter of 'being able to …' (Berg *et al.*, 2006). Based on their results, the authors further developed this conceptual notion to 'being able to be the person I am, used to be and want to be'. This entailed being a living person, a significant person and a useful person. One quote from this study reads: 'You must be fit enough to manage yourself and manage to do things … take care of yourself, make food, go shopping …' (Berg *et al.*, 2006, p.28). Among older Swedish women, familiar routines, such as cooking and shopping, were seen both as a form of exercise and a way to make social contact in everyday life (Sidenvall *et al.*, 2001). Hockey and James (1993) discuss the social constructions of age, dependency and personhood and how these mentally constructed life-course structures are embedded within social contexts and cultures. Thus, being able to care for oneself and being able to shop for food and cook food and meals are part of older people's personhood. The amount of research on older people and food from a life-course perspective has increased during recent decades (Matsson Sydner *et al.*, 2007; Fjellström *et al.*, 2000; Quandt *et al.*, 1997). The life-course perspective on looking at food

and meals in everyday life emphasizes the importance of continuity in older persons' lives. Thus, for many old people, shopping for, planning, preparing and cooking food as well as sharing a meal together with family, relatives and friends is synonymous with maintaining continuity in life. The concept of personhood should also be recognized in relation to health and the ability to shop for and cook food (Berg *et al.*, 2006).

However, if illness and functional problems arise in old age, help and support are essential to obtaining food in everyday life. According to Quandt *et al.* (2001), maintaining food security can be accomplished through self-care or with the assistance of others (informal support, formal service or medical care). Thus, regardless of whether older people continue to live at home, require special housing or are hospitalized, they must still be served meals. It is in these situations that real problems occur concerning the social significance of food and meals. Meals-on-Wheels is an established organization all over the Western world that delivers food to people's homes. Sharkey (2003) is critical of the traditional system and organization of home-delivered meals. In a study among homebound older women who received home-delivered meals, he showed that women who reported food insufficiency were more at risk for the burden of multimorbidity. He goes on to assert the importance of home-delivered meals as a primary source of food assistance to homebound older women, but at the same time stresses the problems inherent in such meals. He suggests that the traditional model of home-delivered meals should be re-evaluated and that measures are to be included to ensure food sufficiency status. Vailas *et al.* (1998) concluded in their study that the correlation between quality of life and quality of health is strong. Important elements of older persons' negative perception of quality of life were reduced food enjoyment (e.g., eating alone) and reduced social satisfaction. Those older persons eating home-delivered meals experienced loneliness, although not as much as could be expected, more than those older persons belonging to the congregate meal group studied.

The will and desire to encourage older persons to become more independent in meal situations have been seen in several studies (Stabell *et al.*, 2004; Sidenvall *et al.*, 1996). However, according to Stabell *et al.* (2004), to make full use of the social event that meals constitute in total institutions, this activity, which involves an interaction between staff and old persons, needs to be developed. Their results showed that when staff encouraged independence in old persons at mealtime, this could also contribute to decreased social interaction between the two parties, because staff did not respond at all and seldom displayed engagement-supportive behaviour. They stress, therefore, that this phenomenon should be recognized.

5.3 Social and cultural implications of food and meals

As pointed out earlier in this chapter, the social implications of food and meals are not only linked to the actual sharing of food at a table and presented as a

meal. The social associations are equally important when people shop for food, prepare and cook food and finally present food in a meal. This is even more prominent an issue when dealing with older people for whom continuity in everyday life is important. Doing what you have been doing all your life, or recognizing a change in your food habits at certain times in your life, could thus symbolize meaningful activities and standpoints in life. Therefore, to fully understand the meaning of the social connotations of food, we need to understand and know about food's cultural system of knowledge. What does planning a meal mean to an older person? What social relationships go through an old woman's mind when she walks among the supermarket shelves choosing food suitable for her husband, her visiting children and grandchildren? How does she reason when preparing a specific meal for herself or her family? The way Carol Counihan discusses the meaning of food is useful in this context (Counihan, 1999). She considers that we give meaning to food in relation to cuisine, etiquette and food rules, taboos and symbols. She defines cuisine as the food elements used and the rules for their combination and preparation. Etiquette and food rules involve customs governing what, with whom, when, and where one eats. However, how one eats food, the actual performance, is not highlighted by Counihan, although it should be. Taboos are the prohibitions and restrictions on the consumption of certain foods by certain people under certain conditions, and symbols are the specific meanings attributed to food in specific contexts. These four fields can also be applicable to illustrating meals as a cultural and social arena. In the following, I will therefore discuss older people's food and meals as part of what I choose to call food's cultural system of knowledge: recognizable foods, habitual everyday behaviour, struggling with traditions, rules and ritual, and finally the meaning of food and meals.

5.3.1 Recognizable foods – cuisine

The way we eat and combine foods into meals is culturally defined (e.g., Mäkelä, 2000). Through our food-related practices, we give specific foods and meals different meanings, and by using different symbols, we can encode and understand the meaning hidden in food and meals in everyday life. For example, if we are living in the Western world and a friend says, 'can I treat you to a burger', we see ourselves in a hamburger restaurant, preferably at lunchtime on a workday, not at a fancy, expensive restaurant in the evening or wearing party apparel at a banquet or a Christmas dinner. On the plate, if there is one, we expect to see French fries together with the burger, not cooked potatoes or rice. The hamburger consists of minced meat, shaped into a patty that is then fried. We do not expect whole pieces of meat cooked in broth. As first pointed out by Mary Douglas (e.g., 1972), who has later been cited by many scholars (e.g., Mäkelä, 2000; Counihan, 1999; Menell *et al.*, 1992), the rules surrounding the meal may be seen as equivalent to a language, with a grammar that gives different meaning to the words and sentences. When old people are offered a specific dish with a specific name, e.g. meatballs, they expect to be served this

dish in a certain way. In Sweden, meatballs are to be fried in a pan; the minced meat is to be mixed with chopped onions and breadcrumbs. Cooked potatoes or mashed potatoes are to be served with the meatballs, as well as gravy and lingonberry jam. Serving rice and a curry sauce with meatballs would not be a success – with stewed chicken, yes, but not with Swedish meatballs! The preparation, combination and serving of different food items and condiments are important if one wishes to keep to culturally established culinary rules (Mattsson Sydner and Fjellström, 2006). Consequently, in the context of elderly care, keeping to the recognizable, the traditional and what one expects when reading a menu is important if we are to ensure that older individuals, who are dependent on others for their food supply, feel comfortable with and enjoy their mealtimes. If we fail to ensure this, the meaning of the meal will be lost, which may negatively affect older people's appetite and the social connotations of a certain meal.

With regard to ageing, it is imperative to regard energy intake in relation to nutrient density, because 'Food that is not eaten is not nourishing' (Fjellström *et al.*, 2000). In the FiLL study, several factors were observed to result in less elaborate meals, which could entail inadequate nutritional intake. Loss of appetite, loneliness, frailty and disease in the last part of life were identified as a transition towards less elaborate meals (Mattsson Sydner *et al.*, 2007). Finding joy in cooking and having the strength to cook are diminished when people became frail, which has also been pointed out in other studies (Gustafsson *et al.*, 2003; Sidenvall *et al.*, 2000).

5.3.2 Habitual everyday behaviour – etiquette and food rules

Older people, as compared to younger people, have been shown to eat with fewer other people present and earlier in the day (de Castro, 2002). In a Swedish study, historical methods and perspectives were used to analyse the development of food and meal habits from the late 19th century to the late 20th century (Fjellström, 1990). It was shown in this study that a change in meal patterns took place during the period in question; yet having a cooked meal in the morning and in the late afternoon (not evening) was still a common pattern among older people in Sweden during the late 20th century. Thus, keeping to a pattern of cooked meals eaten earlier in the day can be seen as maintaining one's cultural heritage.

It is important to recognize the meaning people give to their performance at table. Sharing a table, being part of a social interaction, entails adhering to specific norms and rules in accordance with the prevailing culture. For many old people with functional problems, the fact that they cannot eat without spilling, or handle a knife and fork is a source of shame. This has been shown in several studies (Sidenvall *et al.*, 1996; Jacobsson *et al.*, 2000). Thus, prevailing cultural norms have consequences for how old people view themselves as social beings, as individuals who are or are not accepted by society in an eating situation. The notion of the family meal is embedded in institutions as the norm and the

standard (Sidenvall *et al.*, 1996; Mattsson Sydner, 2002). This phenomenon is emphasized both by staff and guests/patients by encouraging cultural expressions such as behaving at table and being clean, finishing your meal and not wasting food, not complaining about the foods served at meals (Sidenvall *et al.*, 1996).

In another study by Andersson and Sidenvall (2001) on older women with Parkinson's disease, the norm of eating in commensality revealed a negative effect of trying to uphold social interactions at mealtimes. The women with this functional problem experienced stress if fellowship was required, because they could not eat as fast as their table partners. Thus, the social norm of sharing a table is not always what is best for the individual. However, when sharing a table is a possibility, and what the senior consumer wishes, the choice of table partner is important. Being able to choose your meal partners promotes eating more food, according to de Castro (1994). He concluded, based on his study, that people tend to eat more with friends than with strangers. Feunekes and co-workers (1995) demonstrated, however, that this is related to the longer duration of the meal. Naturally, these phenomena are important to keep in mind when serving old people food in special housing or within elderly care. Not only is food important in the meal situation, but also how people talk and what they talk about when forming a group. This was evident in a study by Cheang (2002) among Japanese American older people. He showed that fast food restaurants – a 'third place' in society, meaning an informal friendly public setting where people can get together outside work and the home – were popular meeting grounds for this older Japanese American population. They became part of the group by sharing food, magazines, 'talking story' and 'being there'; however, when they transcended group norms and rituals by, e.g., demanding too much attention for their own stories or not sharing, they were ostracized (Cheang, 2002). Yet this third place was also seen as a sanctuary in which one did not have to follow the rituals and norms established by the Japanese culture.

5.3.3 Struggling with tradition, rules and rituals – taboos

Enjoyment of meals and food is imperative for a person's health and well-being. A specific issue when discussing food and meals concerns the beverages we consume together with food or as part of the meal. In the FiLL study it was found that alcoholic drinks were something old people had little of, or just tasted, as they expressed it (Vas de Almeida *et al.*, 2005). However, among the older population in the northern parts of Europe, as compared to those living in the Mediterranean countries, alcohol was associated with an ambivalent, morally charged relationship. Yet in Sweden, for example, consumption of wine has increased in recent decades to where it is outselling spirits (Selvanathan and Selvanathan, 2005). Thus, wine has become more common as a customary accompaniment to meals and social interaction in Sweden, but the attitudes associated with wine at mealtimes are still negative compared to the cultural beliefs seen in other countries. These differences and changes in cultural beliefs

are important to be aware of, as a given beverage or food can be considered taboo and associated with feelings of shame and guilt among certain age groups and in certain cultures. It would not be surprising if, in the near future, the ageing population in Sweden were to regard wine as a beverage to be served at daily meals, at least in the evening.

Another food item associated with taboos in contemporary society is fat (Counihan, 1999; Oakes, 2004). Old people, too, consider fat the food item they should not eat, or should not enjoy; however, this is clearly a gendered issue (Sidenvall *et al.*, 2000; Gustafsson and Sidenvall, 2002). Fat has become the food that causes most people to feel guilt and shame, because if you eat fat, you are not living up to the societal goal of a healthy citizenry. By rejecting fatty foods, old people can experience that the enjoyment and meaning of the meal are destroyed (Sidenvall *et al.*, 2000). Rejecting fatty foods in old age, especially among the frail, may contradict a healthy and optimal nutritional standard (Nydahl *et al.*, 2003), meaning that old frail people should primarily be encouraged to enjoy food and meals, and to not think about rejecting specific food items.

5.3.4 Meaning of food and meals – symbolism

Food and meals can symbolize many different things, such as commensality, emotions, friendship, happiness, sexuality, adulthood, old age, and so on. They also constitute a symbol of gendered roles. In the European FiLL study it was found that the traditional role women and men had in connection with food in a life-course perspective was as food-givers and food-receivers, respectively (Mattsson Sydner *et al.*, 2007). However, in recent years, it has also been observed that a change in gendered roles in connection with food work is underway. Women, who still live at home but are ailing, may be nourished and fed by their spouses, which forces men to take over the traditional women's role and become food-givers. Losing one's traditional identity could be experienced as both positive and negative. It is important to be aware of this phenomenon when discussing the social significance of older people's meals. It is evident, for example, that especially for old women, cooking for others symbolizes giving the meal as a gift (Sidenvall *et al.*, 2000). Becoming a widow or a widower negatively affected the meaning of food, because the possibility of sharing food with another person was disrupted. Old women who had cooked for their husbands during their entire lifetime suddenly lost their appetites when their husbands died, and this was exacerbated if their children and grandchildren lived far away and were unable to replace the spouse at mealtimes.

As we concluded earlier in this chapter, sharing a meal conveys the identity of belonging to a family. Thus, it follows from this that losing someone with whom one has shared meals, i.e. one's partner, becomes a symbol of no longer belonging. Another way of looking at belonging through food is presented in a study by Quandt *et al.* (2001). By interviewing 145 adults who were over 70 and living in North Carolina, the authors observed that sharing food with friends,

neighbours and acquaintances symbolizes belonging to a community. Food sharing, as in homegrown vegetables, wild foods, cooked foods and meals, was seen as an integral part of community life. By giving away and receiving food, one's identity as an active community member was reinforced, and thereby one's value as a person. These results can be compared to a Norwegian study in which old people considered being healthy to be the same as 'being able' (Berg *et al.*, 2006). Quant *et al.* (2001) also drew attention to the fact that the food sharing phenomenon was based on existing social relations such as families, neighbourhood and churches, and that the foods and meals received, through generalized reciprocity, with little need to repay a food gift directly, could have contributed to the older people's nutritional intake. Although this last aspect of nutritional intake was not documented, it should be taken into consideration when discussing food provision to elders.

5.4 Conclusions and future trends

In summary, being able to participate in the food process, including food choice and culinary rules, to influence the meal situation and the choice of table partners, and being able to share food with others are all part of older individuals' personhood. Safeguarding older individuals' personhood is, therefore, vital in the construction of older people's well-being. Thus, if we are concerned about the social significance of older people's meals, we must ensure that they can take part in at least some parts of the food-to-meal process. It might not be possible for every elderly consumer to actually visit the food shop, but it must be every older person's prerogative to influence his or her food choice, as well as how food is to be cooked, served and shared as a meal. As human beings we are socialized into learning about foods associated with the culture we live in, thus the recognizable food gives us stability and security in everyday life. This is also true for the meal patterns and social interactions at table to which we adapt during our life course, and what we consider to be socially acceptable foods and drinks. A change in food habits at certain times in life, could thus symbolize meaningful activities and standpoints in life. Therefore, to fully understand the meaning of the social connotations of food, we need to understand and know about food's cultural system of knowledge as been shown in this presentation. As we have seen in the present chapter, social isolation can negatively affect nutritional status, but for some older people with functional handicaps, being forced to eat with others can have similar negative effects. In the future, society must focus as much on the social aspects of food as it previously has on nutritional issues in order to fulfil older people's quality of life in relation to food. By addressing these issues by researchers as well as by pensioners' organizations it is more likely that older people's identity as human beings and as members of society will be seen. To take part in the food-to-meal process, however small, is to recognize older people's personhood.

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6

Gender and food in later life: shifting roles and relationships

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Abstract: This chapter sheds light on the enduring importance of food as 'social glue' in old age, and how gendered food practices play a pivotal role in the maintenance of roles and identities in later life. Food practices expose social relations as they reflect and are used to perform social roles and identities. Life events such as widowhood in later life impact on the social roles of older people, which are in turn are reflected in food-related behaviour such as the responsibility for food and food preparation. Continuities and discontinuities are experienced differently by older men and women, and the strategies employed to deal with them reflect perceptions of traditional cultural and gender roles.

Key words: gender, age, marital status, widowhood, new partnership formation.

6.1 Introduction

Whilst most academic literature on food is written from a nutritional perspective, over the last three decades there has been increasing sociological interest in the meaning of food from a social interactionist approach. This interest was stimulated by the burgeoning feminist examination of the gendered domestic division of labour within households (for example Arber, 1993; Oakley, 1975). Cooking and its allied tasks: menu choice, shopping, preparation and clearing up afterwards, continue to be carried out mainly by women (DeVault, 1991; Sullivan, 1997). Since the 1980s there have been changes in the gender dynamics of responsibility for meal preparation associated with age, class, educational level and presence of children within relationship units

(Kemmer, 2000; Warde and Hetherington, 1994). The negotiation of food habits and behaviours of heterosexual couples entering into a relationship, whether cohabitation or marriage, has been investigated by Kemmer *et al.* (1998) and Lake (2006), but less attention has been paid to how food is linked to older people's negotiations and adjustments to life events such as widowhood and new partnership formation. This chapter sheds light on the enduring importance of food as 'social glue' in old age, and how gendered food practices play a pivotal role in the maintenance of roles and identities in later life.

Food practices expose social relations as they reflect and are used to perform social roles and identities. Life events such as widowhood in later life impact on the social roles of older people, which in turn are reflected in food-related behaviour such as the responsibility for food and food preparation. Continuities and discontinuities are experienced differently by older men and women, and the strategies employed to deal with them reflect perceptions of traditional cultural and gender roles.

The chapter firstly examines sociological literature around food and the gendered division of labour in the kitchen, and discusses the sparse literature on ageing, social networks and food behaviours. Secondly, it discusses the methodology of our qualitative research project. Thirdly, it analyses our data to examine traditional notions of age-related feminine and masculine identities and their impact on food related behaviours despite, and as a result of late life-course transitions.

6.2 Gender and meals

For several decades, there has been considerable attention paid to gender segregation in domestic roles, a continuing debate about the relative influence of choice or social structure (Crompton and Lyonette, 2005). Murcott (1982, 1983) in her seminal study of forty working class households in South Wales found that the women in the household willingly did the cooking as part of the marriage bargain: he to provide (a wage) and she to serve (a 'proper meal'). Their duty was performed not only uncritically, but it was viewed as a gratifying accomplishment. Indeed, producing a main meal on the table for his return from work was considered '... a pleasure to cook for him' (Murcott, 1986). The women deferred to the men's taste and preferences, which Murcott argued, reflected patriarchal power and reinforced women's dependence on the family wage earner. Charles and Kerr (1988) surveyed 200 young mothers in the north of England reporting similar findings to those of Murcott in terms of women's prime responsibility for food preparation and their deference to the male partner's tastes. However, both geographical areas had traditionally low female labour market participation and historically gendered division of domestic and public labour. Moreover, as Kemmer (2000) points out, both studies tended to focus on mothers of young children, a period in the life course characterised by economic dependence upon a partner, and women doing most of the domestic duties.

Couples were studied over the period from single to married/cohabiting by Kemmer (1999) who interviewed 22 couples without children, where both partners were in full-time employment in the Edinburgh and Glasgow environs. Her research interest focused on how the shifting economic power relationship between men and women impacts on food preparation behaviours and responsibilities. She found that the women were still generally responsible for the main evening meal, but just under half the couples either shared the tasks (turnabout or together) or, in two couples, the man usually prepared the main meal. What was different was that even in cases where the woman was principally responsible, there was less deference to the male partner's taste than found in earlier studies.

In 2000, Murcott revisited her South Wales findings and asked 'Is it still a pleasure to cook for him?' reviewing literature in the field in the light social changes in the household and family over the previous 20 years by taking the 'OXO Katie' advertisement series as an exemplar of this change. Murcott (2000) found that although men were much more likely to prepare food than in her previous study, they were often 'excessively praised for their efforts' (p. 79), for example, one man who had begun cooking following divorce, one reported 'how he enjoyed being congratulated on his cooking' (p. 81). Nevertheless, Murcott concludes 'on the whole, whether with or without much pleasure, women are still most likely to be cooking for him' (p. 84).

More recently, Lake *et al.* (2006) conducted a follow up of a longitudinal dietary study in Northumberland, which commenced with 12/13 year olds in 1979/80. The informants were surveyed again in 2000/01, aged 32/33; 81 men and 117 women completed the questionnaire. They found that food shopping and preparation remained heavily gendered. Men were generally viewed, by themselves and by the women, as poor shoppers, especially in terms of impulse buying, and only really interested in 'creative' or special occasion cooking rather than the day-to-day tedium of preparing basic meals.

Similar to Kemmer (1999), Lake (2006) found that women were less deferential to their partner's food choices than in previous studies. She noted that common to literature from the UK, USA, Finland and Australia, eating together in the evening was considered the 'ideal', and symbolic of their togetherness. She found that early in the marriage the women were influenced by their husband's preferences, but this decreased as the marriage progressed and ultimately, 'women made the majority of decisions regarding food' (Lake 2006: 10). However, similar to findings of Fagerli and Wandel (1999) there remained some resistance from men to 'healthy diet changes'. Gough and Conner's (2006) small qualitative study found that many of their 24 male interviewees were resistant to changes in their food habits. The men tended to be very cynical about health promotion programmes and reacted against the moralistic terms – preferring to engage with their masculine sense of rationality and autonomy.

6.3 Masculinity, ageing and food

Literature on masculinity has burgeoned over the last decade, but there is still relatively little on older men and masculinities (Meadows and Davidson, 2006). Calasanti (2004) examined how feminist gerontology can inform our understanding of old men and argued that at all ages, gender is relational. Power relations evolve differently between men and women, young and old. Old men are less powerful than young men, but more powerful than old women, with the maintenance of masculinity pivotal to self-identity as men age. It has been argued that there is a 'blurring' of gender in later life whereby men are more likely to show their 'caring' side with grandchildren, for example (Gutmann, 1987). Providing care and undertaking domestic tasks are traditionally the responsibility of women and they generally carry out these tasks 'invisibly'. However, men who care are praised for doing so by friends, family, social and health professionals: the 'Mr Wonderful Syndrome' (Rose and Bruce, 1995), similar to Murcott's (2000) findings that men receive plaudits for creative cooking.

Most of the literature reviewed above has examined young generations and explored food choices and eating habits during couples' transitions including moving in together, embarking upon motherhood, and negotiating duties in the light of other roles in both the public and private spheres. Few have asked to what extent these patterns also occur in old age, and how late life transitions into retirement, ill health, spouse loss or a new cross-gender relationship might alter their food-related behaviours. New dynamics in late life relationships are seldom incorporated into sociological research and yet are integral to the changing shape and experience of the life course. The transitions from worker to retiree and spouse to widow(er) are no longer the only shifts in social roles undergone in later life and for many, will not be their final transition.

Changes in late life relationships and living circumstances impact on the social roles and identities for older people, and food-related activities provide a useful lens through which to explore these. Yet, most research on food and older people is found in medical, biomedical and nutrition journals and tends to portray old age and nutrition as problematic. What is less commonly recognised is how sharing and eating food together remains central to a late life partnership such as marriage. This centrality is augmented on retirement as more meals may be eaten inside the home and with their spouse.

6.4 Growing old together

The cohort of people born between the two World Wars (1918–1939) were brought up in a specific period of time with a common understanding of their experience (Vincent, 2005). The experience of marriage as 'shared biography' is therefore on two levels, the traditional gendered division of labour in society, and their behaviours and consumption habits as a couple unit. Mason's (1987) study examined how gender segregation endures within retired couple relationships:

> The couples each had a great deal invested in their own traditional way of doing things, and the initiation of renegotiation – by definition of proposal for radical change – by either party to this type of relationship would have appeared impractical, pointless and confrontational (Mason, 1987: 93).

Mason argues that although the taken-for-granted roles are not renegotiated at retirement, negotiations do occur within these roles. So, even in conjoint activity, the men 'perform' domestic duties such as (some) cooking and (some) housework, while the women retain the 'management' role (Sullivan, 1997). In retirement, therefore, women continue to dominate the domestic sphere, only relinquishing the responsibility (but sometimes retaining the management role) when they are too ill to carry them out. Davidson (1999) found that some very ill wives were 'tutoring' their husband in cooking skills and ironing; for example, one man commented 'You see, she was still looking after me, even though she knew she was dying'.

6.5 Widowhood and re-partnering

Widowhood is regarded as one of the most traumatic experiences in life (Lopata, 1996). In addition to the grief felt for the lost partner, the individual must adjust to a variety of new roles and tasks that may have previously been performed by their spouse. For older generations, where the division of labour around food-related tasks is usually highly gendered, widowers may face the task of food preparation for the first time in their lives (Bennett *et al.*, 2003). Similarly, widows may be thrust into the alien experience of cooking for one and to their own food preferences (Sidenvall *et al.*, 2000). Freedom from domestic duties is frequently valued by widowed women, but most widowers report feeling less free when they have to fulfil domestic duties formerly carried out by their wife (Davidson, 2001). The shift from spouse to widow(er) is thus intimately tied up with domestic roles such as food preparation and eating meals.

Howarth (1993: 67) examined how the domestic organisation of food may be transformed by spouse loss in later life, arguing that food is 'a vehicle through which to explore and exemplify life course changes'. She found that widowers and widows strive to maintain familiar practices from their former two-person household. These findings show that a transition in marital status in later life results in a re-evaluation of role identities related to food consumption, which often involves individuals trying to maintain identities as well as accepting new ones.

Some older widowed and divorced people form new partnerships which can take the form of marriage, cohabitation or non co-resident relationships (Davidson and Fennell, 2004). Levin and Trost (1999) have identified this last form of relationship as 'Living Apart Together' (LAT). Recent Swedish research demonstrates that meeting together to share food is central to LAT relationships (Borell and Ghazanfareeon Karlsson, 2003). LAT relationships are normally

associated with younger generations and can lead to cohabitation or marriage, but they have not been explored among older people in the UK.

6.6 Life events, gender and food in later life

This section reports eighty depth, semi-structured interviews which were collected as part of the European Food in Later Life[1] project, from 40 men (20 living alone and 20 living with others) and 40 women (20 living alone and 20 living with others), subdivided with equal numbers aged 65–74 and 75 and older in south-east England. All participants were living independently and most were interviewed in their own home, but some received home help or day care (three were interviewed in a quiet room in a day centre). The interviews lasted approximately an hour and half and were carried out by a single researcher. Sources of recruitment included sheltered housing units, religious and social clubs, lunch clubs, day centres, approaching people on free bus services to supermarkets and also a small number contacted through snowballing. The data from interviews were transcribed and analysed using a qualitative software programme (MAXqda).

Participants' accounts of their food lives were discussed in relation to current routines as well as their earlier life and late-life transitions. It was clear from the data collected that social networking and the meaning of meals varied considerably with continuities and discontinuities in the life course. For example, men and women who lived alone after a long marriage were different from those who had lived alone for most of their adult lives. Similarly, long-married people had different social networks from those who had recently remarried/cohabited. People in LAT relationships tended to have 'two routines', one for when they were together and one when they were alone.

We therefore differentiated between these groups which were categorised as: 'always together'; 'newly together'; 'always alone'; 'newly alone' and 'living apart together' (LAT). It was difficult to precisely distinguish between the 'always' and 'newly' but the arbitrary time chosen was 20 years, particularly to reflect the 'always alone' group. However, the vast majority of the 'newly together', 'newly alone' and LAT categories represented periods of less than five years. Table 6.1 provides a breakdown of the sample by living circumstances, age and gender.

All the men and women who had lived with someone for more than 20 years were married (19 women and 16 men), and more than twice as many men as women had lived alone for 20 years or more, seven compared to three. There were more newly alone women (15) than men (9) and more newly together men (co-resident) (4) than women (1). Four men who lived alone had a LAT relationship compared to two women, both of whom were over age 75. Textual

1. European Research Project *Food in Later Life. Choosing foods, eating meals: sustaining independence and quality of life* (2003–2005) (QLK1CT200202447).

Table 6.1 Living circumstance, age and gender characteristics of sample

	Men		Women		All
	65–74 years	75 years and over	65–74 years	75 years and over	
Living with someone					**40**
Long-term partnership = always together	9	7	10	9	
New partnership = newly together	1	3	1	0	
Living alone					**40**
Long-term alone = always alone	5	2	1	2	
Newly alone	4	5	9	6	
Living apart together (LAT)	1	3	0	2	
	20	20	21	19	

extracts from the interviews include a suffix to the pseudonym identifying the living circumstances and age of the quoted participant.

Food consumption and food preparation represent ways of exploring life course changes in later life, revealing gendered norms and differential values. Differences emerged between accounts about food preparation and consumption which suggested that life course continuities and discontinuities of living circumstances and relationships impact on the meaning of meals and domestic roles. We explore the intersection between transitions in late life relationships, social roles and food, and show how continuities of gender shape experience in the face of discontinuities of social relations and roles by examining each of the five living circumstance group identified in Table 6.1.

6.6.1 Always together

The 'always together' group represent a long-term living arrangement. Like younger married/cohabiting couples in previous studies, the older people within this group emphasised the importance of sharing food and meals with their partner. This permeated the organisation of drinks, snacks and meals. Meeting together to eat was an assumed norm and 'part of life' – especially for the main meal of the day, whether midday or evening:

> Well if I was cooking a meal I would expect him to be there for the meal. And if he is out I wouldn't eat my meal until he came back it is not even a case of thinking about it, it is part of life.
>
> Sophie (always together; 65–74 years)

> *Interviewer: And are there occasions when you eat on your own?*
> No very seldom, in fact hardly at all. Even when Julie is out we either eat before she goes out or when she comes back.
>
> Geoff (always together; 65–74 years)

Eating together is pivotal within daily routine for 'always together' older men and women, demonstrating the symbolic importance of waiting for each other to eat. Such was the importance of eating together, that when meals were eaten alone due to other demands on time, the meaning of the meal altered:

> Sometimes I don't bother, I will just have an apple or a banana or something … It is not very interesting sitting on your own eating a sandwich.
>
> Martha (always together; 75 years and older)

This loss of meaning when eating alone is gendered as married men did not describe skipping meals, even smaller ones. Instead the married older men stressed the importance of eating 'something' when hungry. Yet, for married older women, a degree of meaning is attached to meals that means she may forgo the meal when she has no one to share with. Companionship is core to the value of a meal for older married women but for older married men, eating is also essential.

Likewise, the importance of partners eating the same foods was also central to many accounts from the 'always together' group. Despite much evidence of married older women deferring their own preferences to their husband, most respondents in this group emphasised a shared taste in foods. However, these shared tastes may be the result of men's resistance to change:

> But of course when you are married to somebody who only likes meat and three veg, you are a bit put off sort of trying new things out because they never go down well.
>
> Carol (always together; 75 years and older)

For married older women there is a direct connection between enjoyment of food preparation and preparing foods for others, specifically their husband. However, food preparation can also be a monotonous chore:

> *Interviewer: So what is it that you enjoy about preparing and cooking food?*
>
> Not a lot … it's seven days a week, 365 days a year.
>
> Anne (always together; 75 years and older)

Conversely, some long-term married men described a new involvement in cooking since retirement and described this as akin to a hobby:

> Well, what I enjoy about cooking is it gives you a sense of creating something. It's a bit like an artist. You have got your paints and your palette and your canvas and you make something out of it it's just a sense of having accomplished something.
>
> Tom (always together; 65–74 years)

This interest was often reported to have begun post-retirement and tended to be among younger men (65–74). Cooking is turned from a routine, domestic event into a leisure pursuit but interest in cookery is on an 'expert' level rather than a domestic or mundane level.

For 'always together' older men and women, food consumption habits and routine have been developed over a lifetime of marriage. For older women, food preparation can be considered a chore precisely because of the repetitiveness of this daily task. In these households, the bulk of food preparation was performed by the woman: this division of labour was established and continued throughout married life. Furthermore, food preparation is felt by the older women to be a way of showing and receiving love. Many older women stated they would not prepare a food if they knew their husband did not like it. Continuity of roles is present because there is not a discontinuity to challenge them, such as spouse loss.

6.6.2 Always alone

Like the 'always together' group, older men and women who had lived 'always alone' described an established routine and continuity of food habits in the narratives. Because food was not dependent on other people, food was functional:

> Well, it's just 'eat to live' … I suppose it's just routine, you have your breakfast routine, you have a midday routine, you have a tea, it's very routine all the time.
>
> Theresa (always alone; 75 years and older)

Respondents also emphasised that food routines were flexible in order to fit in activities which would otherwise fall over meal times, for example eating a main meal in the middle of the afternoon. Men and women who are 'always alone' do not have another person to wait for to eat, which structures the routine of the long married group. However, food preparation is not always viewed as a 'chore' even if the person lives alone.

> *Interviewer: So you do a roast whether you have visitors or not?*
> Yes I do … I am quite hands on, so I quite like preparing things for a nice meal.
>
> Joyce (always alone; 65–74 years)

Food preferences of others do not have to be incorporated into meals, and cooking may be enjoyable regardless of their living circumstance.

For the 'always alone' older men, food preparation has likewise been a long-term task. Anthony described himself as highly organised, efficient and structured:

> I tend to programme the whole thing so that I eat at 6.30 and so I prepare the things at about 5.30, prepare all the things that I've got to do, put all the things in and go away and appropriate the television set, set that and so on. I like programming things and in due course the pinger goes and there's the meal.
>
> Anthony (always alone; 75 years and older)

For 'always alone' respondents, food preparation is neither a new activity nor an occasional activity, and in contrast to the partnered males, is therefore not described as a 'hobby.' Pride is gained from enjoyment, spending time preparing meals and competency at a task outside the domain of traditional masculinity:

> I like to think that after 30 years I can do a bit of cooking … I do proper cooking, cauliflower cheese, for example, or I have baked salmon, for example … I can do braised beef, a chop which I marinate, as you are supposed to do, in olive oil and all the rest of it and provide at least three vegetables, because I have got an allotment.
>
> Gareth (always alone; 65–74 years)

These older men demonstrate a relationship between masculinity and food. Food preparation may be a challenge to male identity because it is a role traditionally fulfilled by women. However, applying notions of efficiency and technological skill to an account of food preparation communicates a practice similar to that of paid employment, thus raising the status of the activity from domestic chore (which is intrinsically feminine) to proficient employment (intrinsically masculine). For men who have always lived alone, food preparation is built into their sense of masculine identity and used both to perform it and demonstrate the continuity of their identity. For 'always alone' women, the gendered meaning of food is different in comparison to the 'always together' older women, because preparing on behalf of others and in line with the preferences of others is not an aspect of their experience. They share the sense of a continued role but often regarding food preparation as something pleasurable for its own sake. Both 'always alone' older men and women therefore have an established and continued sense of their food roles, which are inherently gendered. It is not the living circumstance *per se* of 'living alone' which shapes experience of food and meals, because older people who have always lived alone are similar to those who have always lived together: it is the continuity of living circumstance and gender identity which mean there is no discontinuity (like suddenly living alone) to make them question food-related behaviour.

6.6.3 Newly alone

The transition of living circumstance and social relations experienced by older people who are 'newly alone' challenges embedded food routines and habits, generating a changed meaning to food, meals and domestic roles. There was a notable emphasis on disrupted food routine, which was often a distressing change that highlighted the loss of social relationships and the commensality experienced with a long-term 'table' companion. Difference between the past and the present was emphasised:

> I wouldn't say I enjoy my food eating on my own as I did when Bob was alive because it would be a social thing.
>
> Katie (newly alone; 65–74 years)

The loss of sharing food together and the loss of particular foods prepared by a spouse were the most frequently described distinctions between past and present. Many of the women described how they lacked routine and incentive to cook now they live alone, and that the focus of their food preparation and food choices was lost.

> My husband died five years ago so things changed rather radically then because we were having more elaborate meals for him.
> *Interviewer: For him?*
> Well I mean we had it together but there isn't the same incentive to go to a lot of trouble when you are on your own, because I have so much to do in the garden, I haven't really time to spend much time indoors.
>
> Audrey (newly alone; 65–74 years)

We know from studies such as Charles and Kerr (1988) that because responsibility for preparing 'family' meals is regarded as a female duty, food preparation is central to a woman's identity as wife and/or mother. 'Newly alone' women explained that priorities with time and efforts in food preparation were now minimised or directed elsewhere. However, this effort was reinvested when they had visitors, such as family or friends to eat in their home.

For the 'newly alone' men, food and meals also changed markedly following the disruption of a change in living circumstances. For these men the major change was that they were suddenly responsible for all meal preparation whereas previously they had either shared a part of the routine or not contributed at all.

> She used to make these big paellas in a great big pan and also as I said the omelettes … I miss the things she cooked.
>
> David (newly alone; 65–74 years)

Clearly, it would be disingenuous to say that at mealtimes, the women missed the company and the men missed the food service, but in our sample, men were polarised in terms of taking responsibility for their food preparation. One group were *enthusiastic* and independent in regard to their new food life while another group were *reluctant* to put effort into food preparation, finding food a difficult element in their life as a man living alone.

For the *enthusiastic* group of 'newly alone' men, independence and not being a burden were extremely important in their approach to food and meals:

> It didn't take me many days to get around – people, neighbours were kind for a few days over important things … but quickly I was able to show them that I was independent … I don't want to be a burden to my family or to myself.
>
> Ralph (newly alone; 75 years and older)

Central to this and other similar quotes, is a pride in the control they hold over their food and meals and the knowledge that they are 'coping'. This emphasis on independence was not found in the accounts of the 'newly alone' women, because food preparation is not a new role they have acquired but one

which continues in a different form. Whereas responsibility for food is relinquished by the 'newly alone' women, these *enthusiastic* 'newly alone' men adopt it and take pride in it. This change in identity is further reflected in the descriptions of food-related tasks by the 'newly alone' *enthusiastic* men. They apply a functional, practical and structured approach to their food routine, and suggest a satisfaction gained from the task:

> I work hard on a Friday, I go into the market and I get my fish and the fruit and whatnot and then I come home and stew the fruit and fillet the fish and make the soup. I am not lazy.
>
> Roger (newly alone; 75 years and older)

Both 'newly alone' men and women tended to emphasise the importance of ease of preparation. However, for these *enthusiastic* men, the emphasis is not on the lack of incentive of a person to cook for but on being economical both with time and resources, echoing the accounts of the 'always together' and 'always alone' men. Their emphasis on independence and self-sufficiency was not found in the food accounts of the widowed women, we argue, because these are qualities more associated with a sense of masculinity. These men adopted a new (but still masculine) identity as food preparer for themselves, and approached this new role as a skill they have gained, using food as a vehicle to perform and construct gender. This is different from 'newly alone' women who regard their role of food preparer as something they lose rather than celebrate following widowhood.

In contrast, for the *reluctant* group of 'newly alone' men, food is a poignant reminder of how their lives have changed. Food preparation is a chore they find boring to complete, difficult and different to their previous food life. The structured and efficient enthusiasm of the men cited above is absent in place of total reluctance:

> I can eat anything okay, but as long as I am eating something, then I am not starving; that is my theory … Half the battle, I think, is to get a meal someone else has cooked. It is put in front of you. It is taken away and they do the washing up. *I have had a meal*.
>
> Bernie (newly alone; 75 years and older) [our emphasis]

Their new living circumstance has created a crisis of assumptive norms wherein gendered divisions of labour have been broken, leaving this group without motivation or skill to prepare a meal. 'Getting someone else' is key, because this creates continuity from the past, and more specifically, a continuity within gendered assumptions. *Enthusiastic* widowers emphasise masculine identities of independence, efficiency and self-sufficiency by building these into their new food preparation activities; *reluctant* widowers seek continuity in their masculinity by reinforcing their dislike of undertaking 'feminine tasks' and finding ways to get someone else to prepare food, put it in front of them, take it away and clear it up.

Therefore 'newly alone' men and women differ in the way food preparation is disrupted following spouse loss. For 'newly alone' women, the meaning of

food preparation changes from something they do for others to something they must now do for themselves alone. For 'newly alone' men the meaning of food preparation changes from something which has always been done for them, to a new task which may be a challenge to their established, gendered identity. Older men tackle such challenges in varying ways but seek to create a continuity of masculinity, or as Connell (1995) argues, different masculinities come into play.

6.6.4 Living apart together (LAT)

Reflecting Swedish findings (Borell and Ghazanfareeon Karlsson, 2003), the four older men and two women who are 'living apart together' (LAT) tended to meet in the woman's home and it was usual for her to prepare the meals on these occasions. Furthermore, it was also usual that the woman cooked the meals which were eaten together, even when they took it in turns to meet in each other's home or met in the man's home. This demonstrates that a separate household partnership does not mean a freedom from traditional gendered divisions of labour implicit in marriage.

The LAT older men echoed the experiences of their widowed 'newly alone' counterparts, describing a preference for having food prepared for them by someone else. When alone, eating because of need was their incentive to cook, but meals prepared by their LAT partner were enjoyed because they were both more delicious than they could prepare for themselves, and because they were prepared by another:

> No I don't enjoy cooking. No. It is just something to eat when I am hungry I can't be bothered to go to any trouble with recipes or anything like that. I get that when I go to her, she loves doing it … no, I just do it because I have to.
>
> Archie (LAT; 75 years and older)

> *Interviewer: Do you join in with the cooking there?*
> Well sometimes. Betty seems to like cooking though.
>
> Oswald (LAT; 65–74 years)

Older women in LAT relationships accepted their preparation of meals when together and explained this as being in order to allow her partner a rest from his food preparation at home:

> Yes, although he is a very good cook and I think occasionally he will do it here but he does it all the time at home.
>
> Serena (LAT; 75 years and older)

This reflects an assumptive world in which it is 'given' that when together as a couple the woman should take on the role of food preparation. The LAT men perceive their partner to enjoy this task and the women perceive it as normative that they should do this: both Serena and her partner prepare their own food for themselves during the week, but *he* is deserving of the weekend break from food preparation.

Often the male LAT partner would pay for ingredients, do the washing up, pay for meals out, or prepare smaller meals such as snack lunches or breakfast in order to reciprocate for the woman's work in preparing the main meals:

> I go and wash up while she's cooking, because of course the dirty dishes pile up, so I wash up in her kitchen, but I don't do anything else.
>
> Anthony (LAT; 75 years and older)

Older LAT women prepare quick and light meals for themselves when alone during the week, but so-called 'proper meals' when their partner was present. Like widowed women, the word 'incentive' is used to describe how cooking for themselves alone is different from cooking for others:

> I would just have a bit of salad … but then I have a gentleman friend who comes … so my routine is very different – you know just cooking for one – but then I cook for two on Friday, Saturday and Sunday which I do full meals. All meat and chops and vegetables and that sort of thing.
>
> Serena (LAT; 75 years and older)

> Well, it's nice when you're cooking for somebody, and when you're on your own it's not … because, well, the incentive is not there … But I never mind cooking for him.
>
> Beth (LAT; 75 years and older)

Eating together is an integral part of the means by which these relationships are conducted and expressed. For the female LAT respondents, the effect of re-partnership on their experience of food and meals is the value of company at meal times, whereas for the male LAT respondents, value is gained through both having company and through having a person who prepares food for them. This reinforces the findings for the 'always together' and 'newly alone' groups, which demonstrate that older women value company at meal times and miss this aspect of their marriage following widowhood, while older men miss both company and meal content.

6.6.5 Newly together

Some older people also experience a form of discontinuity in living circumstance by entering a new co-resident partnership designated the 'newly together' group. These five remarried respondents emphasised a new shared food routine. However, eating alone was a salient recent issue for these individuals and was drawn on for comparison to their new circumstances:

> Eating on your own is deadly. … Eating with people is much more pleasant, much nicer, rounder, compared with being by yourself.
>
> Bill (newly together; 75 years and older)

> Yes, she has been seventeen years by herself, and I have been seven. And we find that eating together is rather nice.
>
> Jim (newly together; 65–74 years)

Like the LAT group, food preparation is generally performed by the woman in the relationship:

> My wife does it now … I am quite happy to have people cook for me. I can cope on my own if I have to but I don't really have to so I don't worry.
>
> Harold (newly together; 75 years and older)

Pragmatism is evident here as the males all emphasise that they *can* cook, if they need to; when identity reverts to being a cohabitating couple, so gendered food identities revert to the traditional domestic divisions.

For the only female remarried respondent in our sample, her change in circumstances was also regarded as significant in terms of companionship at meal times:

> I feel sorry for people who have to eat on their own … It is companionship as much as anything. Sitting down together and talking.
>
> Madeline (newly together; 65–74 years)

For men, new partnerships bring the bonus of companionship and food prepared by another, but for women it is principally the benefit of companionship, since their cooking is taken for granted. Gendered norms regarding roles around food preparation are assumed by both the older men and women, and these direct and shape the experience of the new partnership as women re-adopt food preparation roles and men happily accept them.

6.7 Discussion and conclusions

The experience of the life course is changing for many older people. The increasing prevalence of new partnership formation creates new experiences in later life which are seldom incorporated into sociological research. As later life becomes increasingly diverse it is important to understand how age, gender and discontinuity in relationships and roles intersect. We found that changing partnership dynamics in social relationships, such as widowhood or new partnerships, were reflected in the meanings of food preparation and consumption. Continuity and discontinuity of living circumstances shape and direct how the social context of meals are experienced by older people. Continuity in living circumstances and partnership status whether long term partnered or long term alone, means stability in roles and identities in relation to food behaviours. Discontinuity in living circumstances means a disruption of established roles and relations, demanding a re-evaluation and renegotiation of identities in relation to food consumption and preparation.

Food is a gendered issue in later life. For older men and women, both partnered and alone, food preparation occurs within a framework of gendered assumptions. Older women defer personal food preferences to men and regard preparing food on behalf of others as their central incentive for preparing food and meals, supporting early research findings with younger age cohorts (Murcott, 1983; Charles and Kerr, 1988). Therefore, following widowhood, motivation to prepare main meals is reduced, confirming findings of Swedish research (Sidenvall *et al*., 2000).

For men, changes in social roles and relationships present new domestic challenges. For those who have always lived alone, food preparation is a continued role integrated into their sense of identity, whereas for 'newly alone' men, food preparation represents a new task which must be incorporated into their identity. Similarities between men in all groups in the sample illustrate how masculinity is reflected and performed in relation to food. Some men build on intrinsically masculine notions of expertise, proficiency and economy to present their food preparation as a proficient employment rather than a domestic chore. For other men, getting someone else to prepare food indicated maintenance of traditional domestic food roles.

Re-partnering in later life is reflected in food-related activities. In both cohabiting and separate household relationships, the role of food preparation is performed by the older woman, and in LAT relationships, usually in the home of the female partner. This is not openly negotiated between new partners but occurs based on assumptive gender norms of both older men and older women. Gendered attitudes to food-related roles are implicit in accounts and behaviours and inherent in the construction of roles within the new relationship.

The data presented in this chapter suggest a less explicit negotiation of food-related activities amongst older re-partnered men and women than those reported by Kemmer *et al.* (1998) from a cohort of young newly cohabitating partners. However, concurring with Kemmer *et al.*'s findings, for both remarried and LAT partnerships in our sample, eating together was implicit, symbolically important and central to their new relationship. For older people engaged in new relationships, eating together is of additional salience because of their previous experience of eating alone following widowhood.

Gender shapes and directs new experiences at times of transition in social roles and relationships in later life. Although assumptive norms are taken from past roles, gendered norms are vulnerable to change on partnership loss. However, they remain powerful in shaping new roles and relations, and are restored in new partnerships, generating some continuity in late life transitions.

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7

Older people's consumption of alcoholic beverages: the social significance and health implications

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Abstract: This chapter focuses on the social and cultural meanings of alcohol drinking as well as the health implications of its consumption by older people. Alcoholic beverages are part of daily life across the world, from ancient civilizations to present times, with important economic, social, cultural and religious roles.

Alcohol metabolism and its effects depend of several factors, such as age, gender and health status. This might be a particular issue to consider when looking at alcohol drinking of older people. Measurement of consumption and daily acceptable intakes is difficult to achieve since they depend on many factors and on the methodology used in research.

Many associations have been found on what concerns alcohol drinking and health, but research as been focused mostly on the negative effects of alcohol, although scientific evidence of some associated benefits also exists. Excessive intake of alcoholic drinks exerts toxic effects in several organs due to both ethanol and the compound that results from its metabolization (acetaldehyde). More recently, other possible risks and benefits of drinking alcohol were found by research but those are not specific to the older consumer.

Key words: alcoholic beverages, elderly, social significance, health implications.

7.1 Introduction

7.1.1 Alcohol as a beverage

Alcoholic beverages originated thousands of years ago when the alcoholic fermentation of cereals, fruits, and other vegetables occurred by chance. The earliest descriptions about vine cultivation, the use of wine as well as beer production, are found amongst the civilizations of the eastern Mediterranean. Indeed, three to four millennia ago wine already represented economic, social and religious value for Egyptians, Greeks and Hebrews.

The distillation of fermented drinks leading to spirit production only occurred much later, in the XIII century and has been associated to Villanova, a scholar who worked at the University of Montpellier (France). Over time, in most societies and cultures, the drinking of alcohol has been associated with rituals, special occasions and ceremonies as well as being a part of daily life and daily meals.

In chemical terms, alcohols are a large group of organic compounds. Ethanol (CH_3-CH_2-OH) belongs to this class and is the main psychoactive ingredient of alcoholic beverages. This compound is obtained by fermentation of sugar by yeast (primarily by *Saccharomyces cerevisiae*) and is present in concentrations between 3% in beers and 12–14% in wines. Spirits, obtained by distillation of fermented beverages, have a higher concentration of ethanol (above 40%). In spite of not being considered a nutrient, alcohol yields 29 kJ (7 kcal) per gram (Table 7.1).

Table 7.1 Nutritional composition of some alcoholic beverages, per 100 ml

	Energy (kJ)	Alcohol (g)
Fermented alcoholic beverages		
Beers (bitter)	124	2.9
Ale	123	2.8–3.7
Stout	94–126	2.6–3.3
Cider	152–197	3.8–5.5
Red wine	274–283	9.2–9.6
White wine	302–394	9.1–9.6
Rosé wine	294–299	8.7–8.8
Sparkling white wine (dry/sweet)	290–448	8.8–9.0
Champagne	315	9.9
Madeira wine	644	17.0
Port wine	562–678	15.5–17.0
Vermouth (dry/sweet)	453–631	13.0–13.9
Distilled alcoholic beverages		
Wine spirit	1289	44.0
Brandy	1031	35.2
Liquer	1099–1438	19.8–31.8
Spirits 40% volume (mean) – Gin, Rum, Whisky, Vodka	919	31.7

Source: Adapted from *Miscellaneous Foods*, 4th supplement to McCance and Widdowson's *The Composition of Foods*, 1994 and *Tabela da Composição dos Alimentos Portuguesa*, 2006

7.1.2 General metabolism

The absorption of alcohol starts shortly after being ingested by passive diffusion in the gastric mucosa, where around 30% of alcohol is absorbed (Fig. 7.1). The remaining 70% is mostly absorbed in the duodenum (65%) and in the colon (5%). Absorption duration may vary between 15 to 20 minutes and three hours, depending on whether the drink was taken without any foods or as part of a meal.

The maximum blood concentration of alcohol is reached around 30–60 minutes after ingestion and it is diffused to all organs and cells according to their vascular nature and water content, mainly to the liver, brain, kidneys, heart and muscles. As a water-soluble compound, alcohol has more affinity with the body water components. Its blood concentration reduction occurs at a fixed rate of 0.1–0.2 g/l and by hour, most of it (90–95%) being metabolized in the liver. Although quite constant, this rate may be influenced by individual, genetic factors and adaptation due to enzymatic induction. Only 5–10% is excreted without being metabolized, by the kidneys, lungs, skin and saliva. In the liver, the enzyme alcohol dehydrogenase, oxidizes ethanol to acetaldehyde.

There is a general consensus that there are differences between men and women in what concerns alcohol physiological effects. These may be explained by differences in the enzymatic system, body water content and body size. Owing to their smaller body size and lower water content, alcohol concentration in women will remain higher in comparison to men of similar weight. Women metabolize alcohol at a slower rate than men, so this compound remains in their tissues for a longer period, and they are also more susceptible to the adverse effects of alcohol at high levels of consumption when compared to men (Harding, 1999).

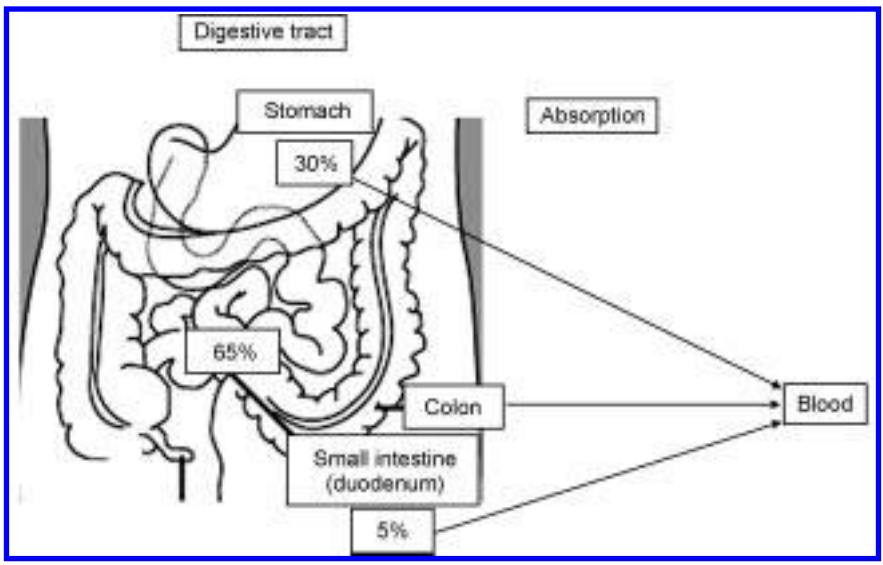

Fig. 7.1 General metabolism: alcohol absorption in the digestive tract.

Excessive intake of alcoholic drinks exerts toxic effects in several organs (liver, brain, heart, kidneys, pancreas, amongst others) due to both ethanol (which remains in the blood stream until complete metabolization by the liver) and acetaldehyde. The liver metabolizes this latter compound to free radicals and acetate, which will be incorporated in the Krebs Cycle. The effects of alcohol may be acute or chronic, due to long-term excessive drinking. As alcohol is not stored in the body, its excessive consumption disrupts the metabolic systems and has been associated with health hazards that include liver cirrhosis and various types of cancers (Sulander *et al.*, 2004).

With increasing age, there is a decline in the ability to metabolize alcohol, thus increasing its adverse effects. Also, the changes in body composition due to ageing, with a decrease in muscle mass and total body water, and an increase in fat mass, lead to higher alcohol blood level for similar quantities drunk. As a result, the upper limit of moderate drinking is lower for men over 65 than for younger men (Meister, 1999).

7.1.3 Acceptable intakes

There is a general agreement that a moderate intake of alcoholic beverages, namely red wine, has several health benefits. However, most scientific boards have not established recommendations for alcohol intake, which means that this section will discuss acceptable intakes, i.e. intakes which have been shown to have positive health effects.

Estimates based on epidemiological studies suggest that for an average adult man the optimal level of alcohol intake ranges from 10–19 g/day and the non-harmful (or moderate) level is about 30–40 g/day. For an average woman the respective levels are <10 g/day and about 10–20 g/day. However, these estimates of the optimal and non-injurious levels of alcohol intake are valid only for the 'average adult'. The concept of 'optimal' level of alcohol intake is based on the findings that mortality due to specific causes, is lower among light drinkers than those who drink more heavily or who do not drink at all. However, for those diseases which do not show such a 'J-shaped' or 'U-shaped' (Fig. 7.2) relation between degree of risk and level of alcohol intake, it is not possible to speak of an optimal level (ILSI, 1999).

In general, there is no distinction between younger and older adults when referring to alcohol consumption. This is the case of the United Kingdom national guidelines that establish for men an intake of three to four 'standard units' of alcohol per day, (average of 1.7 to 2.25 drinks/day), based on a non significant risk increase. For women, recommendations are lower and defined as two to three standard units (average of 1.1 to 1.7 drinks/day). No values are specifically indicated for older adults, although it has been discussed that the limits for this age group should be lower than for adults (Lang *et al.*, 2007a).

In contrast, countries such as the United States, Italy, New Zealand and Australia have set maximum values for the elderly. The US National Institute on Alcohol Abuse and Alcoholism (NIAAA) recommended for people aged 65

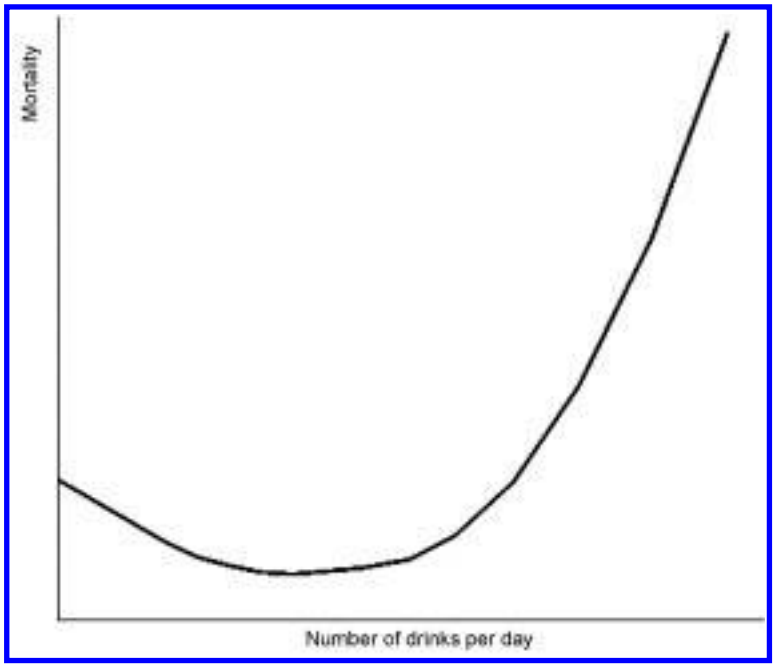

Fig. 7.2 J-shaped curve: mortality vs. number of alcoholic drinks per day.

years and over to limit their intake to one drink per day, which is half of the daily recommendation for the adult men aged less than 65 years. Also, Italy established a 25% reduction in consumption, when compared to younger adults. New Zealand and Australia advise older people to drink less than adults but without setting any levels (Lang *et al.*, 2007a).

7.2 Alcohol consumption by elderly populations

7.2.1 Measurement issues

There is no universal definition of what constitutes a 'unit of alcohol' or a 'drink' and, in fact, the amount of a 'drink' and the volume of alcohol in each 'drink' varies intra and inter-culturally. Moreover, there are different concepts of 'light', 'moderate' and 'heavy' drinking. This may be illustrated by a review of 28 scientific papers, in which the lower limit of moderate intake ranged from 4.5–50 g/day and the upper limit from 24–80 g/day. Thus, these variations introduce limitations to the analysis, interpretation and comparability of data, with negative implications for a clear identification of the amount/frequency associated to the benefits and risks of drinking alcohol (ILSI, 2001).

The analysis of alcohol-associated risks/benefits is influenced by methodological aspects, errors and bias in the quantification of alcohol consumption as well as by individual (age, sex, body composition, health status), socio-economic and lifestyle (diet, physical activity, smoking) factors (WHO, 2004).

7.2.2 Consumption data

The HALE project (Healthy Ageing: a Longitudinal Study in Europe) combines data from the populations studied in the SENECA (Survey in Europe on Nutrition and the Elderly: a Concerted Action) and FINE (Finland, Italy, Netherlands Elderly) projects. SENECA and FINE collected longitudinal data that explores the effects of a healthy lifestyle on mortality and morbidity in old age. Data was collected in ten different European countries, enabling the comparison between areas with different lifestyles and food habits.

Both studies aimed to assess the protective effects of the so-called Mediterranean diet, physical activity, smoking behaviour and alcohol consumption (Knoops *et al.*, 2004). A total of 2,044 men and 1,049 women aged 70–90 years were included in the analysis which showed marked gender and geographical differences in alcohol intake. Men drank on average between 21 g/day in northern European countries and 31 g/day in southern ones, whereas on average the amounts drunk by women were quite similar between north and south: 6 g/day (Knoops *et al.*, 2004).

Data from the second SENECA follow-up showed that between surveys (1989–1993) most elderly groups decreased their alcohol intake, with the exception of Danish and French men and Belgian and Dutch women. Italian, Portuguese, and French men showed the highest alcohol intake (all above 20 g/day). Women drank much less in all centres, the highest amount found in Italians (11.5 g/day) and French (7.6 g/day) elderly (Tables 7.2 and 7.3). Polish elderly (both men and women) had the lowest ethanol consumption. It is worth noticing that the energy provided by ethanol was in general low for women (except for French and Italian) but in the case of elderly men it could contribute up to 10% of the energy (in Italy).

The consumption of alcohol was higher in the towns where regular drinking is socially acceptable and where wine was the source of alcohol (Moreiras *et al.*, 1996).

The latest US Health Survey (2006), reported a decrease in alcohol consumption with age. As age increased, the percentage of adults who were current regular drinkers decreased. 'Current regular drinking' was defined as having had 12 drinks or more in his/her lifetime and at least 12 drinks in the past year (US Department Health Human Services, 2007).

Data from alcohol consumption in England (2005), revealed that for both men and women, the number of units consumed in an average week decreased with age when comparing the youngest (16–24 years) to the oldest (65 and over) group; 24% of men reported drinking over 21 units (average)/week and 13% of women over 14 units (average)/week, above the governmental definition of 'sensible drinking' (England, 1992). When compared to 1998, this constituted a slight decrease for men but similar for women. The proportion of older people reporting this consumption was lower among the oldest age group when compared to the 16–24 age group.

Regarding chronic drinkers, this last report also found variations with age. Men aged 16–24 were more likely to drink in excess of an average of 50 units a

Table 7.2 Daily dietary intake of alcohol (g) in elderly men (mean, s.d.) by towns in Europe and the USA (source: Moreiras *et al.*, 1996)

				Percentage of energy	
Town	N	Mean	s.d.	Mean	s.d.
Hamme/Belgium	68	19.5	29.0	5.2	6.6
Roskilde/Denmark	57	13.7	16.4	4.4	5.4
Haguenau/France	56	25.0	20.7	7.7	5.2
Romans/France	70	17.1	16.0	5.9	5.4
Padua/Italy	69	32.5	28.8	10.3	8.7
Culemborg/Netherlands	52	10.1	11.3	3.2	3.8
V. F. Xira/Portugal	77	18.9	26.8	6.5	8.7
Betanzos/Spain	35	16.7	26.3	4.3	5.8
Yverdon/Switzerland	71	12.8	11.9	4.7	4.2
Coimbra/Portugal	13	31.5	36.2	8.2	7.0
Marki/Poland	47	3.1	5.9	0.6	1.2
B-L-Portstewart/N Ireland	32	2.7	5.9	0.8	1.8
Mansfield (Connecticut)/USA	11	5.3	10.3	1.6	3.1

week (9%) than men aged 65 and over (3%), and this was also true for women (NHS Information Centre, 2007).

Portuguese National Health Surveys showed an increase in the proportion of drinkers from 50.4% in 1998/1999 to 53.8% in 2005/2006. The higher percentage of drinkers was found to be the 45–54 years old (74.4%, in 2005/2006).

Table 7.3 Daily dietary intake of alcohol (g) in elderly women (mean, s.d.) by towns in Europe and the USA (source: Moreiras *et al.*, 1996)

				Percentage of energy	
Town	N	Mean	s.d.	Mean	s.d.
Hamme/Belgium	61	6.4	15.9	2.3	5.3
Roskilde/Denmark	58	6.0	10.4	2.7	5.1
Haguenau/France	53	7.6	7.0	3.0	2.8
Romans/France	72	3.3	5.0	1.5	2.2
Padua/Italy	66	11.5	11.2	4.3	4.1
Culemborg/Netherlands	69	3.7	9.8	1.5	4.4
V. F. Xira/Portugal	80	0.7	3.8	0.3	1.8
Betanzos/Spain	47	5.0	8.5	1.7	2.8
Yverdon/Switzerland	79	3.7	4.8	1.8	2.5
Coimbra/Portugal	14	2.0	4.4	1.0	2.2
Marki/Poland	73	0.2	0.7	0.04	0.2
B-L-Portstewart/N Ireland	38	1.6	3.6	0.6	1.3
Mansfield (Connecticut)/USA	18	4.6	10.5	1.7	3.9

When comparing people that referred to have drunk 'at least an alcoholic beverage' to the ones that did not drink alcoholic beverages at all, in the twelve months preceding the interview, there was also a decrease in the percentage of consumers as age increased. Consumers of alcohol represented 60.7% of the 65–74 years old and 43.2% in the oldest group (85+ years). There were consistently more men drinkers than women in all age groups: 81.7% and 43.7% for the 65–74 years old; 69.7% and 30.6% for the 85+ years (INSA, 2007).

7.2.3 Excessive consumption

Alcohol abuse is a topic of special concern in geriatrics. Several population-based cross-sectional surveys have shown that the percentage of men and women consuming alcohol decreases after 65 years, as does the average amount of alcohol consumed for those who drink. However, most studies were carried out in the USA and cannot be generalized to other countries, or even to other USA elderly populations, due to biological as well as cultural differences. Data from a longitudinal study in a population of Japanese men aged 60+ years found a similar decline after the age of 70 years. Still, it was concluded that although a decline in alcohol consumption existed for this population, several subgroups showed important differences. Trajectories of alcohol consumption appear to be closely dependent on life events, health status, gender and employment. The trajectories should be investigated in adult drinkers and accompanied until old age to achieve consistent information from their drinking habits (Gee *et al.*, 2007).

A systematic review of the utility of self-reported alcohol screening instruments by elderly people concluded that detection of alcohol use disorders in the elderly might be of great interest but should not replace a more complete examination (O'Connell *et al.*, 2004). As many studies rely on screening instruments, possible errors can occur. Further investigation is needed to clarify whether there is a real decline in consumption or if this is only apparent and due to possible bias in the available data.

The assumption that alcoholic use disorders have a lower prevalence in older people is possibly wrong, since it has been reported that some situations are not detected and/or diagnosed. Underdetection and misdiagnosis are common for several reasons. First, there is a lack of information on medical records from older people; it is also evident that there is a cultural tendency to neglect alcoholic beverage consumption at these ages; and there is a lack of a clear definition of weekly alcohol intake. The concomitant use of medication can also have a high impact for this at-risk population due to drug–alcohol interactions. In some situations these interactions may be more relevant to the adverse effects on health than the amount of alcohol consumed in itself (O'Connell *et al.*, 2003).

7.3 Social significance of alcohol consumption across cultures

This section addresses the determinants (i.e., environmental, societal, cultural and religious) of alcoholic beverage consumption. Behaviour associated with alcohol consumption is complex and a comprehensive approach needs to be taken. People's culture and society have great influence as they are inherent in the environment, involving symbolic functions and being part of transitional and festive rituals.

The cultural and social research on drinking alcohol aims to understand the different contexts in which this behaviour occurs and to address how, what and why people drink. There is a large cross-cultural variation in drinking patterns, as in some societies alcohol consumption is associated with positive beliefs and harmonious drinking behaviour, whereas in others alcoholic consumption is associated with violence and anti-social behaviour (SIRC, 1998). Previous research has dichotomized attitudes and behaviours towards drinking as *Temperance and non-Temperance* drinking cultures. The former, also called 'dry', 'Nordic' or 'ambivalent', as in the UK, the USA, the Scandinavian countries and Australia, often present inconsistent beliefs and expectations with regard to alcoholic beverage consumption and are associated with high levels of alcohol-related problems. The latter, also defined as 'wet', 'Mediterranean' or 'integrated', as observed in the Mediterranean and some South American countries, present, in general, positive beliefs and expectations concerning alcohol drinking and present fewer alcohol-related problems (SIRC, 1998).

However, beliefs and expectations of a given culture change over time. There is evidence that the *Temperance*/*non-Temperance* drinking cultures seem already to be changing, and mixed attitudes have been observed in the different countries. The influence of some northern 'ambivalent' cultures has been noticed in southern European countries, including an increase in alcohol-related problems.

It is also important to understand where alcohol is consumed due to the often social nature of the activity. In most societies drinking alcoholic beverages is confined to designated environments that reflect attitudes towards alcohol. Also in the *Temperance*/*non-Temperance* perspective, cultures with a positive and integrated attitude tend to favourably accept 'open' drinking environments, while the others tend to confine this attitude to 'closed' surroundings (SIRC, 1998).

Religion also expresses its influence in alcohol consumption, either integrating or proscribing alcoholic drinks. In the Catholic religion, red wine symbolizes the blood of Christ and is central to the Mass ritual. On the other hand, alcoholic beverages are proscribed by the Islam and abstention plays an important role in Muslims' daily life (Dietler, 2006).

Gender studies about alcohol consumption have documented that men are more often drinkers, consume more alcohol, and are usually more likely to have drinking problems. They also tend to talk about alcohol more frequently than women. Unacceptability of alcohol consumption was in some countries much

more implicit in women's than in men's narratives. It should be pointed out that heavy drinking by women is less socially accepted and tends to be more underreported and hidden than men's.

It seems that in countries in which there is greater gender equality, the gender differences in alcohol consumption are smaller. This was found in northern European countries. On the contrary, the largest gender differences were found in the developing countries. This might be attributed to the cross-sectional nature of the data. Bloomfield and colleagues refer to the necessity for research in this field since several hypotheses were not clarified. The question of whether differences in alcohol consumption are due to a higher consumption by women in countries where there is greater gender equality, whether these are due to lower consumption by men, or even to both, remains unclear (Bloomfield *et al.*, 2006).

In a recent multi-centre qualitative study, narratives about drinking alcohol from 644 old people living in the community, from eight European countries, provided valuable information about attitudes, beliefs and behaviours around alcohol and alcohol consumption (Vaz De Almeida *et al.*, 2005). This study found social influences regarding alcohol drinking to be quite evident in countries (e.g., Sweden) in which strong norms about drinking (when, where, with whom, how and how much) exist. Alcoholic beverages are so embedded in some cultures that elderly from Portugal, Spain and Germany didn't talk about 'alcohol' when referring to wine or beer. They tended to name the drink, whereas those who were abstainers used the generic term 'alcohol' or 'alcoholic drink' (Vaz De Almeida *et al.*, 2005).

Alcoholic beverages are an important part of the ritual when friends or relatives share a meal and drinking in the company of others is perceived as more appropriate than drinking on your own or outside of meals (Vaz De Almeida *et al.*, 2005). This stresses the importance of social drinking and how it is viewed in these societies where sharing is acceptable, whereas drinking on your own is viewed as a deviation from the social norm.

Although the cultural meaning and framing of drinking are reported to resist change, the actual frequency of drinking and heavy drinking occasions may change (WHO, 2002). In our previously mentioned work (Vaz De Almeida *et al.*, 2005), several narratives registered that as some habits changed, alcoholic consumption habits, also changed. This seemed to be the case in wine-producing countries (e.g., Portugal and Spain), which were also traditionally wine consumers, where consumption of other types of beverages such as beer or spirits was reported. In countries like Poland, where distilled drinks were common in the past, only few narratives claimed they had never drunk any strong alcohol like vodka.

Also, meals and other eating occasions experienced some changes, but wine at the main meal is still the most common alcoholic beverage in Mediterranean countries. On the other hand, in the northern European countries, wine began to be included more frequently and the strong alcoholic beverage consumption was less mentioned. Beer or other alcoholic beverages were also found to be drunk

during other food events, such as snacks during the afternoon (Vaz De Almeida *et al.*, 2005).

It is worth noting that in societies with an ambivalent, morally charged relationship with alcohol (such as the UK), 'celebration' is used as an excuse for drinking; whereas in societies in which alcohol is a morally neutral element of life (such as Mediterranean countries), alcohol is strongly associated with celebration but not seen as a justification for every drinking occasion (SIRC, 1998).

Health status, digestive problems and chronic diseases are important determinants of alcohol consumption, but this differed across the European countries, as negative or positive associations between health status and alcohol consumption were found. Contradictory findings between real alcohol consumption and spontaneous comments show that the negative impact of alcoholic beverages on health are well known by the older population. However, alcoholic beverages such as wine or beer are so firmly linked to culture that drinking habits are assumed as a very common and natural habit within the daily routines. This reflects the complexity of drinking behaviour and how scientific knowledge and culture may take opposite views when referring to alcohol consumption.

The constraint for women's drinking is a cultural finding not yet explained, but some authors attribute it to the different physiologic capacity to metabolize ethanol. However it is most likely that there is also a socio-cultural component to the explanation (SIRC, 1998).

7.4 Health implications of drinking alcohol

Wine consumption, one of the characteristics of the Mediterranean diet, is thought to be one of the major factors behind the positive effects attributed to this eating pattern. People who follow the Mediterranean diet, which includes wine in moderate amounts at meals, are considered to be healthy and live long (Trichopoulou, 2004).

In order to determine the health consequences of alcohol consumption, scientists have tried to define levels of consumption (light, moderate and abuse) in association with the health risks or benefits of the different drinking patterns. As previously discussed, the concepts applied in research vary depending particularly on the methodology defined for each study, therefore introducing large variations in results, which hinders the establishment of associations.

The main association of alcohol consumption and health is the well known relationship between alcohol consumption and mortality, following a J-shaped or U-shaped curve, as previously mentioned. A review of the literature shows that a protective effect occurs at a level of consumption of one to four drinks, whereas five or more drinks per day result in an increased risk. Still, we have to stress that the literature does not define consistently what should be considered 'moderate' and 'heavy' drinking. Also, the definition of moderate drinking presented by the different studies is not always consistent with dietary guidelines from the countries where research has been made (Gunzerath *et al.*, 2004).

The potential risks of alcohol consumption are clearly linked to a heavy drinking pattern. As other substances, ethanol becomes toxic when consumed in a high quantity. High consumption of alcoholic beverages is harmful to health and there are some well-documented consequences of the health implications of excessive drinking (Fig. 7.3).

7.4.1 Cardiovascular health

Several studies have shown that light to moderate alcohol consumption may decrease total mortality, the risk of coronary heart disease, and ischemic stroke in middle-aged and elderly people (ILSI, 1999; Lin *et al.*, 2005). Data from the Cardiovascular Health Study, a study involving people aged 65+, suggests that alcohol 'may exert a protective effect by favourably altering hemodynamics or influencing other factors that affect either the development or clinical presentation of congestive heart failure' (Bryson *et al.*, 2006). This relationship refers to a moderate consumption of alcoholic beverages (1–6 drinks), but the authors clarify that further investigation is required to establish the exact mechanism. One of the specific findings of this study is the effect on the carotids with a decrease in the degree of atherosclerosis.

To address the potential problems and benefits of alcohol on cardiovascular health three different health conditions have to be distinguished: coronary heart disease (CHD), stroke and hypertension.

Coronary heart disease (CHD)

There is scientific evidence that alcohol exerts a protective effect against CHD when ingested in moderation as it influences several risk factors. It increases high-density lipoprotein (HDL) cholesterol levels, with a short-term inhibitory effect on blood clotting (Meister, 1999). The review of the bibliography from the past two decades shows a growing number of epidemiologic studies that have documented an association between alcohol consumption and lower risk for CHD, which is one of the most relevant causes of death in the developed countries. One of the mechanisms explaining the protective effect of alcohol in CHD is the hypothesis that alcohol protects against peripheral vascular disease. In this condition, blood flow to the extremities is impaired due to narrowing of the blood vessels. So, the peripheral vasodilatation due to alcohol intake could be the mechanism behind alcohol consumption. Research data on the effect of alcohol consumption and peripheral vascular disease, however, remains controversial (Anon., 2000).

Other effect of alcohol consumption, which is in fact the most commonly mentioned, is the increase in HDL cholesterol levels, which contributes to prevention of CHD. Blood HDL cholesterol is a lipoprotein with a well-known protective action against atherosclerosis and cardiovascular diseases in general.

Atherosclerosis is basically a chronic inflammatory process that affects the arteries of different vascular beds. It is characterized by the thickening of the layers from these blood vessels, with loss of elasticity. The atheromatous plaque

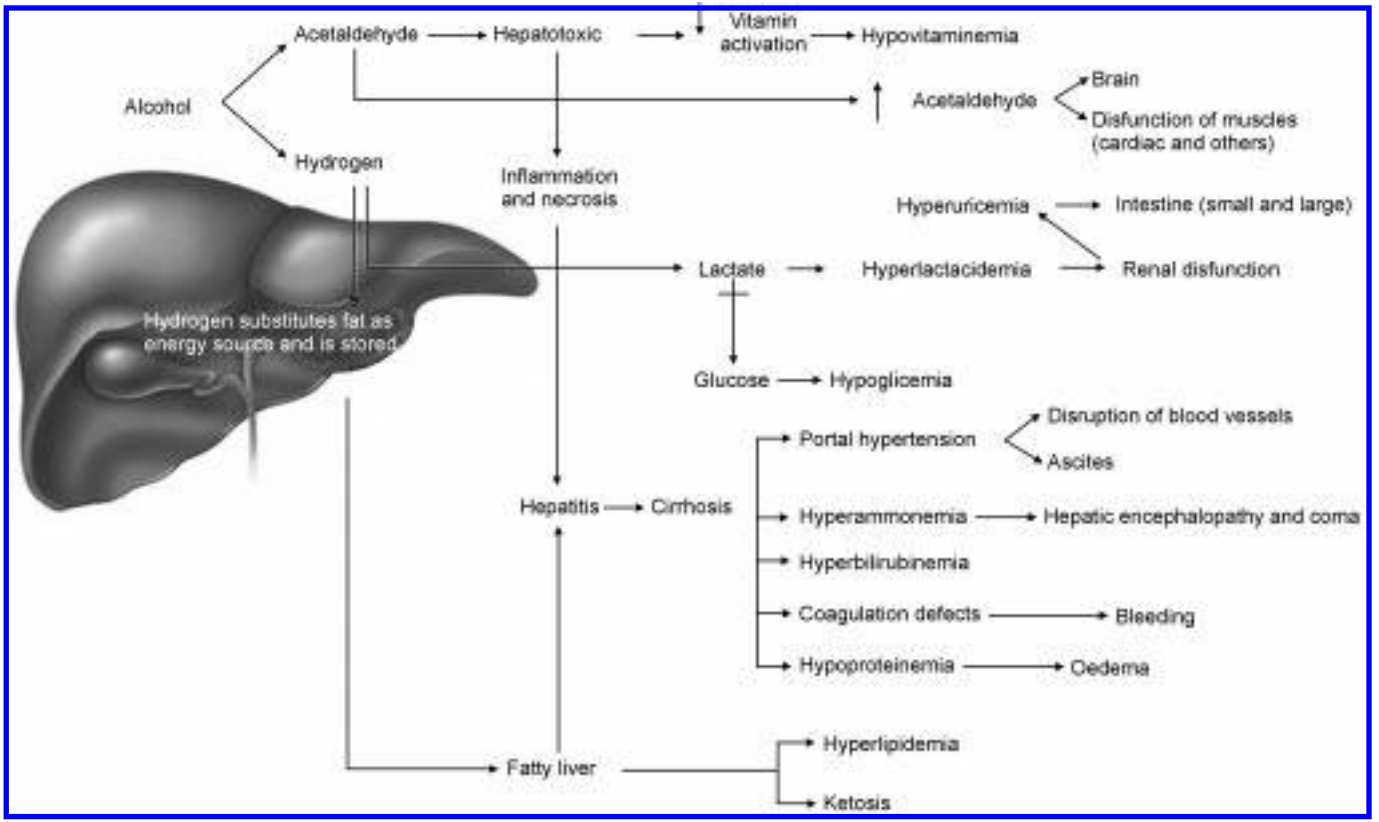

Fig. 7.3 Consequences of excessive alcohol consumption.

is the basic lesion and is composed of lipids, fibrous tissue and inflammatory cells. This chronic disease mainly involves the medium-sized arteries, resulting in ischemic heart disease (IHD), cerebrovascular disease (CD), or peripheral arterial disease (PAD).

Blood HDL cholesterol removes the excess cellular cholesterol to the liver for its metabolism and excretion, and thus impairs the development of atheromatous plaque. Alcohol is also known to affect the coagulation system, by reducing platelet aggregation and fibrinogen concentration, and increasing plasminogen activators (Da Luz and Coimbra, 2001). These contribute to allow blood to flow normally and reduce the risk of developing cardiovascular diseases.

In general, a light to moderate consumption of alcoholic beverages is associated with a lower total mortality in middle-aged and elderly men and women (ILSI, 2001). A recent European project on elderly (HALE project) concludes that: 'In the elderly, non-smoking and moderate alcohol consumption lower mortality risk' (Knoops *et al.*, 2004). Moreover, results from the Cardiovascular Health Study support the inverse association between alcohol intake of 14 or more drinks per week and risk of CHD in older populations (Mukamal *et al.*, 2006). Most studies have shown an 'apparent protective effect against CHD', whatever the level of assumed 'moderate' alcohol consumption, for both men and women (Anon., 2000).

On the contrary, heavy drinking patterns, that is an intake of five or more drinks per day, may lead to impaired ventricular function and subsequently to the development of cardiomiopathy. Alcoholic cardiomiopathy is often a complication of alcoholic abuse during a long period of time and is related to the dose of ethanol ingested during lifetime (Gunzerath *et al.*, 2004).

In spite of the benefit of light to moderate alcohol consumption on total death rates and cardiovascular mortality, Agarwal and colleagues recommend that currently non-drinkers should not be encouraged to start drinking alcohol (Agarwal, 2002). The US and UK guidelines to promote cardiovascular health suggest that alcohol consumption in 'moderation' can have a protective effect, if consumption is limited to 2–3 drinks per day (ILSI, 2001).

Stroke

Stroke is a severe disruption of blood supply to the brain, which can result from the blocking or narrowing that occurs in blood vessels in cerebrovascular diseases. There are two types of stroke, the one that results from a blockage of a blood vessel (ischemic), and the one that happens due to a disruption of a blood vessel (hemorrhagic).

Alcohol-related hypertension can result in both kinds of stroke. If the two types are analysed separately, some findings suggest a positive effect for alcohol consumption and ischemic stroke, while the opposite effect is found for hemorrhagic stroke (Anon., 2000). This happens because mechanisms that lead to the two types of stroke are different (Meister, 1999). Behind the positive effect on ischaemic stroke is the increase of HDL cholesterol levels and a short-

term reduction of blood clotting by alcohol consumption. However, an association was found between heavy drinking and increased risk of stroke, particularly for women.

Hypertension

The mechanisms behind how hypertension causes the development of atheromatous plaque remain controversial. One hypothesis is that an excessively high blood pressure would damage the endothelium and increase its permeability. Also, it could induce the rupture of the atheromatous plaque or the proliferation of smooth muscle cells. Some clinical trials have shown that a decrease in arterial blood pressure is associated with significant reductions in the rate of some clinical complications of hypertension, such as stroke and coronary events (Da Luz and Coimbra, 2001).

Hypertension is a risk factor for stroke and CHD. Research in this field suggests that there is an association between heavy drinking and increased blood pressure for both men and women. However, the relationship between alcohol consumption and high blood pressure still has to be confirmed, as the literature reviews remain inconclusive (Anon., 2000; Meister, 1999).

Although alcohol consumption is pointed especially as contributing to elevated blood pressure and associated complications, two patterns of drinking should be distinguished for a more comprehensive analysis. In fact, heavy alcohol intake is known to have a negative impact on health by promoting hypertension, but a light to moderate intake is recognized to be beneficial on CHD and ischaemic stroke. This means that alcohol cannot be considered as harmful or beneficial towards blood pressure without taking into consideration the individual's drinking patterns. The more negative effect of alcohol consumption that has been associated with hypertension is hemorrhagic stroke (Harding, 1999).

7.4.2 Effects in the nervous system

The fact that psychiatric disturbances are associated with vascular disease was a motive to examine the relationship between cognitive decline and alcohol consumption. The Rotterdam Study which included people of 55 years and older, found a reduced risk of dementia in participants who reported a light to moderate alcohol consumption, regardless of the alcoholic drink consumed. A population-based prospective study in Bordeaux (France), designed to assess the relationship between wine consumption and dementia also revealed an inverse relation (Ruitenberg *et al.*, 2002).

Research has being inconclusive until now when referring to the effects on Alzheimer disease (AD) and macular degeneration (Gunzerath *et al.*, 2004). It seems that there is an association between light to moderate intake of wine and a decreased risk of dementia and Alzheimer's disease in genetically predisposed individuals (Luchsinger *et al.*, 2004).

Possible mechanisms involved in this protective effect are still being

investigated. It is possible that alcohol might act through reduction of cardiovascular risk factors; and also that it might have a direct effect on cognition through release of acetylcholine in the hippocampus (Letenneur *et al.*, 2004).

On the other hand, alcohol and its metabolites affect the central nervous system, but the effects of heavy drinking patterns differ from moderate intakes. The prolonged or excessive intake of alcoholic beverages is associated with an increased risk of dementia due to neurotoxic effects (direct action) or other causes, such as malnutrition and trauma (external causes). Although this evidence seems unquestionable, two types of dementia should be considered when discussing alcoholic beverages and its effects: Alzheimer's dementia or disease (AD) and vascular dementia (VD). Recent research has revealed an association between moderate alcohol consumption and decreased risk of development of any type of dementia or the VD dementia (Gunzerath *et al.*, 2004; Letenneur, 2004). Several studies report the positive effects of light-to-moderate drinking (one to three drinks per day), irrespective of the alcoholic beverage (Letenneur, 2004).

Also, it has been suggested by some authors that moderate alcohol consumption can reduce the risk of developing AD. However, this association does not imply a causal link and the unknown effect of different types of alcohol calls for further research (Letenneur *et al.*, 2004).

General well-being and cognition were also investigated in a recent study. Lang and colleagues observed that for middle-aged and older people, men and women, a moderate consumption pattern of up to two drinks per day was associated with better cognitive health than was abstinence. This population also had better subjective well-being and fewer depressive symptoms (Lang *et al.*, 2007b). Nevertheless, benefits of moderate alcohol consumption on well-being and cognitive function have been poorly explored and require further investigation.

Long-term abuse of alcohol is related to development of the Wernicke-Korsakoff syndrome, a disease also called alcoholic dementia. This disease is caused by the lack of vitamin B1 and is usually associated with malnutrition due to excessive consumption (Letenneur, 2004).

7.4.3 Effects on bone

The effects on bone differ depending on the dose, duration and pattern of alcoholic beverage use. An acute intoxication interferes with calcium metabolism by enhancing its urinary excretion, leading to a drop in blood calcium levels. Also, there is an increase in blood magnesium and its excretion by alcohol consumption. As a result of these mineral changes, bone formation is depressed. So, acute intoxication has a short-term effect on bone metabolism (ILSI, 1999).

Moderate alcohol consumption effects remain controversial. Some studies showed a positive association between moderate alcohol consumption and risk of hip and forearm fractures, especially in older women. On the other hand,

some researchers did not find adverse effects on bone density (ILSI, 2001), and a positive association with bone metabolism of elderly women was even found in other studies (Ilich *et al.*, 2002; Mukherjee and Sorrell, 2000).

The mechanisms behind the positive effect seem to be the alcohol-induced conversion of androgens to estrogens (by aromatization), which is the only source of estrogens for post-menopausal women. It may also inhibit the development of osteoclasts and bone rebsorption, affecting bone remodelling; and it is associated with parathyroid hormone (PTH) and 25 hydroxy vitamin D (25-OHD) levels, known to play an important role in bone metabolism.

A review of several population group studies reported that a history of high intake of alcohol confers a higher risk for future fractures, independently of bone mineral density which contributes to the controversy (Kanis *et al.*, 2005).

7.4.4 Digestive tract diseases and cancers

Chronic heavy alcohol consumption is unquestionably related to liver diseases and mortality (Anon., 2000), as liver plays a major role in the metabolism of alcohol and other toxic substances (ILSI, 2001). Excessive alcohol consumption causes liver inflammation (hepatitis) and cirrhosis. It can also lead to fatty liver disease (steatosis), one of the most common lesions found in alcoholic patients, which consists of the deposit of lipids on hepatocytes (Harding, 1999).

The risk of developing these complications depends on the level of consumption, and there is some evidence that women are more susceptible than men to the cumulative effects of alcohol on liver (Anon., 2000). Also, heavy drinking patterns and hepatitis C are associated with mortality from liver-related causes (Jansen, 2002).

The amount of alcohol needed to cause liver damage and disease depends on an individual's susceptibility to alcohol (Meister, 1999). However, it has been suggested that detrimental effects begin at levels as low as 14 drinks per week for men, and 7 for women. Even at moderate intake levels, alcohol seems to enhance the carcinogenic potency of other hepathotoxins. Also, it induces CYP2E1, an enzyme that metabolizes some procarcinogens to carcinogens. Heavy alcohol consumption can also impair hepatic regeneration (Gunzerath *et al.*, 2004).

There is scientific evidence that reactive metabolites of alcohol, such as acetaldehyde, may also be carcinogenic. The negative consequences of alcohol consumption may be mediated through the production of prostaglandins, lipid peroxidation, generation of free-radical oxygen and, as a solvent, alcohol enhances the entrance of carcinogens to the cells (AICR, 2007).

Heavy drinking patterns may also lead to cancers from the accessory organs of the digestive tract and other types of cancers of the digestive tract itself (stomach, colon and rectum) (Anon., 2000).

There is a quite well-documented association between chronic gastritis (inflammation) and alcoholic beverage consumption. In spite of the fact that neoplasic development has not been established as a direct consequence of

alcohol consumption (Anon., 2000), research suggests that ethanol is not a carcinogen by standard laboratory tests, but animal experiments showed that given by mouth it may act as a co-carcinogen in the development of cancers in the non-glandular (fore) stomach, but not in the glandular stomach or pancreas.

According to documented studies, alcohol seems to contribute in some way to the cancer of the gastric cardia and, by leading to chronic pancreatitis, it might also contribute to development of pancreatic cancer. Nevertheless, no direct association between alcohol consumption and cancers of stomach and pancreas has been firmly established, since the evidence remains inconclusive (ILSI, 2001).

The relation between alcohol consumption and colorectal cancer is also uncertain and controversial (ILSI, 2001). Some research has associated this cancer with high levels of alcohol consumption but the development of cancer was found for levels not much above the limits of moderate drinking (Meister, 1999). Research amongst middle-aged and elderly men and women concluded that high alcohol consumption and smoking habits are associated with an increased risk for colorectal cancer. It is assumed that approximately half of the colorectal cancer cases may be preventable by avoiding tobacco and alcohol in older age groups (Otani *et al.*, 2003).

7.4.5 Cancers of the head and neck

There is evidence that alcoholic beverage consumption is implicated in the development of cancers of the head and neck, such as in the mouth, pharynx, larynx and oesophagus (Anon., 2000; ILSI, 2001). The risks are associated with the presence of ethanol and acetaldehyde, and seem to increase directly with higher consumption levels (Gunzerath *et al.*, 2004; ILSI, 2001).

7.4.6 Breast cancer

The links and mechanisms behind the association of alcohol consumption and breast cancer remain unclear and controversial (Gunzerath *et al.*, 2004; ILSI, 2001). The most likely relationship is found with a heavy drinking pattern, but even this can be compromised by unknown factors (ILSI, 2001). Recently, the American Institute for Cancer Research (AIRC) following an extensive review on alcohol and breast cancer, concluded the existence of consistent evidence of a dose-response relationship for alcohol consumption and both pre- and postmenopausal breast cancer (AICR, 2007).

7.4.7 Other possible risks and benefits

Although other risks and benefits of alcohol drinking have been established for adults, no information exists for the elderly. Therefore, we will briefly address these issues as they constitute areas for future development in the relationship between old age and alcohol.

Reduction of risk for developing diabetes mellitus type 2 has been studied. The mechanisms are not (yet) clear (Gunzerath *et al.*, 2004; Meister, 1999), but it is postulated that alcohol consumption can reduce or increase the risk, depending on the pattern of consumption. Once more, moderation is associated with positive, and heavy consumption with the negative effects. Studies also revealed decreased incidence of heart disease for people suffering from diabetes if alcohol was ingested in moderate amounts (Howard *et al.*, 2004). Further research is needed to determine the long-term effects of alcohol consumption on glycaemic control and other implications in diabetes mellitus.

Some studies report an inverse association between moderate alcohol consumption and some of the conditions that characterize the metabolic syndrome, namely a beneficial effect on glycaemia in women. This syndrome is usually associated with obesity and diabetes, and predisposes to CHD (Gunzerath *et al.*, 2004).

Although some of the conditions related to obesity are linked to a benefit concerning moderate alcohol consumption, heavy drinking patterns will affect body function in several ways and have harmful effects. Excessive alcohol intake can raise triglyceride levels and blood pressure, leading to heart failure and increased energy intake. The higher energy consumption may lead to obesity and, also, to a higher risk of developing diabetes.

Still, the way in which alcohol consumption can affect weight and energy balance is yet poorly understood (ILSI, 2001), and both situations of weight gain and obesity or weight loss and malnutrition are associated with drinking. The harmful effects of excessive consumption to malnutrition are explained by the fact that there is a proportion of the daily energy intake from alcoholic beverages and a poor intake of other nutrients. Those nutrient deficiencies concern especially vitamins A, B (folic acid, B1, B6 and B12), E (tocopherol) and some minerals (magnesium, calcium, zinc, selenium and iron). In the more severe cases of alcohol abuse energy-protein malnutrition can also be found (Seal *et al.*, 1999). Besides malnutrition, heavy alcohol consumers that have deficient diets may be more susceptible to carcinogenesis in the different tissues and organs (AICR, 2007).

The protective effect of alcohol may be stronger in individuals with a particular phenotype or genotype. One of the most widely known conditions that is dependent on the genotypic characteristics is the alcohol and acetaldehyde metabolism, which determines the individual's capacity to detoxify alcohol (ILSI, 2001). To determine the genetic variability that influences a person's reaction to alcohol will lead to the design of individualized therapies, thus constituting a promising field for researchers and health professionals alike.

7.5 Conclusions

The elderly constitute a very heterogeneous group of people as far as age span, health, fitness, social class, and living circumstances are concerned. All these factors may influence alcohol consumption and, in turn, are influenced by the

amount and patterns of drinking alcohol. Like other physiological changes that occur with ageing, the metabolism of alcohol takes place at a slower rate, with implications for health and well-being.

In addition to other changes that occur as we become older, it is also important to investigate whether the social norms related to alcoholic consumption also differ from adulthood to old age.

In populations with excessive alcohol consumption it is difficult to distinguish between the effects of ethanol in itself and those that can result from other factors, such as smoking, drug abuse, and unbalanced food habits. These can act synergistically, thus intensifying the harmful effects of each one. Research in this area is complex and hindered by methodological issues. However, in spite of several limitations and contradictory findings, moderate alcohol consumption seems to have a positive effect on health at the same time as alcoholic beverages are of social significance for human populations, including the older age groups.

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Part II

Extending functionality into later life

8

Undernutrition: diagnosis, causes, consequences and treatment

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Doctors and nurses frequently fail to recognize undernourishment because they are not trained to look for it.

J. E. Lennard-Jones, 1992

Abstract: Undernutrition is one of the most common and devastating conditions in the older population. In this chapter we summarize the causes of undernutrition and its consequences for health, including specific vitamin and mineral deficiencies. The issues of diagnosis and treatment of undernutrition are also discussed.

Key words: undernutrition, protein-energy malnutrition, vitamin deficiency, elderly.

8.1 Introduction

Undernutrition is one of the most common and devastating conditions in the older population and has been defined amongst others as 'different deviations from the normal nutritional state'. The diagnosis is made with different methods. Data on the prevalence of protein-energy malnutrition depend on the methods and cut off values applied, but is estimated to be between 5 and 10% in community dwelling people above 70 years of age up to 30–65% in institutionalized people of that age (Guigoz 2006; Visschedijk and Schols 2006; Silver *et al.* 1988). Clearly, prevention of malnutrition is an important issue among older adults. Also, identifying older persons at risk and making an early diagnosis is crucial for effective intervention. In this chapter we will summarize the causes

of undernutrition and consequences for functionality. Parameters most relevant for the diagnosis of undernutrition will be discussed, in addition to the frequently observed more specific vitamin and mineral deficiencies. Assessment and treatment of undernutrition is not easy and often a multidisciplinary approach is necessary. We will finish this chapter with a look at ethics in the treatment of undernutrition.

8.2 Causes and consequences of undernutrition: the downward health spiral

Inadequate nutritional intake is the predominant cause of undernutrition in older persons. Loss of appetite that occurs with age, the anorexia of ageing, has been defined by Morley and Silver as 'the physiological decrease in food intake occurring to counterbalance reduced physical activity and lower metabolic rate, not compensated for in the long term' (Silver *et al.* 1988). Anorexia may result from either physiologic or pathological causes in older persons. The causes have been discussed by Donini in Chapter 3 and are summarized in Morley's mnemonic: 'MEALS ON WHEELS' (Table 8.1; Morley 1997). In addition to inadequate intake, impaired digestion (caused by medical conditions, e.g. atrophic gastritis or gastrointestinal tumours) and increased requirements during chronic diseases and acute infections may cause undernutrition. On the one hand, undernutrition and decreased physical activity in old age have an effect on functions such as muscle function, immune function, bone health, sensory functions and cognitive performance. On the other hand, impaired functions affect nutrition behaviour and physical and social mobility, with as a consequence inadequate dietary intake leading to a downward health spiral (Egbert 1996). The question is how to counteract this spiralling downward health in a timely manner.

Table 8.1 Mnemonic for causes of anorexia of ageing: MEALS ON WHEELS

M	Medications (digoxin, theophyline, fluoxetine)
E	Emotional causes (depression)
A	Alcoholism
L	Late-life paranoia
S	Swallowing problems
O	Oral problems
N	No money
W	Wandering and other dementia-related problems
H	Hyperthyroidism
E	Enteral problems
E	Eating problems
L	Low salt (in general therapeutic diets)
S	Shopping and cooking

Source: Morley (1997)

8.3 Diagnosis of undernutrition

From a medical perspective it is crucial to diagnose undernutrition at an early stage. Visschedijk and Schols (2006) as well as Omran and Salem (2002) mentioned four categories of most relevant parameters in the diagnosis of undernutrition. We will discuss these parameters below.

8.3.1 Anthropometry

Body weight loss is considered the most important indicator of undernutrition. A loss of 10% in 6 months, 7.5% in 3 months or 5% in one month is considered as very serious, due to a direct relation with morbidity and mortality (Sullivan *et al.* 2004). Conditions that may affect the interpretation of weight changes, such as oedema, ascites and loss of body parts, should be considered. In older adults three major forms of weight loss are distinguished:

- sarcopenia results from a loss of muscle mass due to ageing and decreased physical activity (Rosenberg 1997)
- cachexia, a loss of lean body mass as a consequence of infections or other diseases
- wasting, a loss of lean and fat body mass due to serious shortages in the food supply.

Also, in some older adults dehydration can be a major cause of weight loss.

In the absence of previous recorded weight, comparison with desirable weight in addition to reported changes in weight might be helpful. A body weight 20% below the desirable weight is considered an indication of poor nutritional status.

The body mass index (BMI) is calculated by dividing body weight in kg by the square of the height in m (kg/m^2). This parameter may give an indication of under- and overweight in addition to information on body composition at least in younger adults. A low BMI in older adults indicates sarcopenia. However, even a low BMI ($< 22\,kg/m^2$) may mask increased fat mass, and a higher BMI may mask the so-called sarcopenic obesity (a low lean body mass and high fat mass). An accurate identification of sarcopenic obesity requires more precise methods, such as bioelectrical impedance. For older adults BMI is also difficult to interpret due to the inability of the patients to stand erect or because of chronic illnesses that affect stature. An alternative recommended measurement for height is knee height (WHO 1997). Because of the age-related changes in body composition, the cut off values for over-and undernutrition are also different in older adults. A BMI value below $22\,kg/m^2$ is considered a risk value in older adults (WHO 1997).

Other measurements which may give a rough indication of muscle mass and fat stores respectively are measurement of the mid-arm circumference with a flexible tape and the triceps skin-fold measured by a caliper. Mid-arm muscle area (MAMA) can be derived from the combined data and has shown to be a predictor of mortality risk in older adults (Allard *et al.* 2004). However, the

measurements are difficult to standardize. Calf circumference is a measurement indicating muscle mass.

Bioelectrical impedance (BI) is a more sophisticated tool to measure body cell mass (BCM). This part of the body includes muscle mass and viscera, which are considered the vital compartments of the body. Volpato *et al.* (2004) showed that a high BCM is associated with significantly less mortality risk in a 4-year study. The BI is increasingly used, but takes more time than a simple (well-standardized) body weight measurement.

There are a number of other tools, including computed tomography, MR imaging, dual photon absorptiometry and others, which are very costly, require special training and are difficult to justify in clinical or outpatient care settings.

8.3.2 Evaluation of dietary intake

Information on dietary intake can reveal suboptimal fluid or nutrient intake and an imbalanced food choice. Additional questions on shopping habits, times, duration and supply of meals may also give indications for either causes or treatment of undernutrition. Use of supplements should be included in the dietary evaluation, as well as the time and type of medicines used. The dietitian can use different methods for collecting dietary information:

- *Food records* for two or more days are easiest to conduct in long-term institutions, where staff can help with the administration.
- *The dietary history method* can be useful in outpatient clinics, if the older adult has no cognitive problems. If the patient does not cook, the person responsible for the food preparation should also be available for answering questions. The dietary history method may take a long time (about 1 hour).
- *Food frequency questionnaires* are quick and easy, if the diagnosis is fixed to specific nutrient problems such as calcium, zinc, iodine, vitamin A, D or vitamin B12.
- *A 24-hour recall method* is often less helpful, due to the short period – which may not be representative for the diet of the patient – and the often impaired short-term memory of older adults.

In interpreting the results of the dietary anamnesis we should realize that older adults consume less than younger adults. Owing to changes in metabolic rate and physical activity, energy expenditure and thus energy requirement is reduced. From the literature it is well known that especially elderly in long-term care may have a very low energy intake. This may fall below 6.3 MJ or 1500 kcal in men but more often in women. De Groot *et al.* (1999) have shown that with such a low energy intake it is not only difficult to maintain body weight, but also to obtain an adequate supply of micronutrients.

8.3.3 Biochemical evaluation

For the diagnosis of undernutrition biochemical indices have been used in clinical as well as research settings. However, the use of these parameters is

questionable, because all of them are also influenced by pathological processes and stressful situations. The increasing levels of cytokines during such processes suppress the production of many of these indices and thus cannot be interpreted as markers of the nutritional status only. Table 8.2 shows the effect of age and non-nutritional factors on variables considered as biochemical markers of the nutritional status. We summarize their usefulness below.

- *Serum albumin* is used as a screening indicator for nutrition when its value drops below 38 g/L, even though reference values may differ between labs. Limitations in using the serum albumin level as a marker for undernutrition are its long half-life (18 days), measurement errors that occur in the presence of dysproteinemia or uremia and lack of specificity. Serum albumin is an

Table 8.2 Biochemical parameters of the nutritional status: effect of age and non-nutritional factors

Indicator	Effect of age	Other influences*
Albumin	Small decrease	> Paraproteinemias < Posture, cytokines, nephrotic syndrome, heartfailure, acidosis
Prealbumin	None observed	> Renal failure, steroids < Inflammation, stress, iron deficiency, end-stage liver disease
Transferrin	Gradual decrease	> Iron deficiency, acute hepatitis, estrogen < Neoplasms, nephrotic syndrome, end-stage liver disease, some antibiotics
Retinol binding protein	Small decrease in men Small increase in women	> Renal failure, acute liver injury < Stress, zinc and vitamin A deficiency, hypothyriodism, end-stage liver disease
C-reactive protein	None observed	> Trauma and sepsis < None observed
Insulin growth factor-I	Strong decrease (35–60%) from 4th decade onwards	> Renal failure < Inflammation, stress, auto-immune diseases, hepatic failure
Urine creatinine	Decrease	> Protein rich diet < Renal failure, steroid
Total lymphocytes	Small or no change	< Stress, sepsis, neoplasms, steroids
Serum cholesterol	Increase: controversial is a decrease as early sign of terminal decline	> Hypothyroidism, saturated fat < Liver disease

* > are factors leading to increased values; < are values leading to decreased levels.
Table based on Visschedijk and Schols (2006) and Omran and Salem (2002).

important marker of the protein pool. Levels may decrease with conditions affecting its synthesis in the liver or accelerating its loss as in the case of the nephrotic syndrome. Cytokines result in 'third-spacing' of albumin into the intravascular space. There are more factors which affect the diagnostic value of serum albumin, nevertheless the level is considered a reliable prognostic tool. A low level is indicative for decreasing functionality, increased morbidity and mortality (Zuliani *et al.* 2001, Visser *et al.* 2005).

- *Prealbumin* is also synthesized in the liver. Its serum level is widely used as a marker, because of its shorter half-life (2 days) and superior sensitivity in diagnosing acute malnutrition. Also prealbumin values return faster to normal values after nutritional repletion. In the presence of pathologies affecting prealbmin levels (see Table 8.2) the trends of the values are more indicative than absolute values. The normal range is considered to be between 160 and 360 mg/L (Fidanza 1991) Again, cytokines lower the circulating levels.
- *Transferrin* is another variable formed in the liver and takes care of iron transport. It has been used as a marker of the nutritional status in hospitalized patients and for other frail elderly people (Lesourd *et al.* 1996). However, the correlation of transferrin levels with anthropometric or other parameters of malnutrition is not very clear. It increases with insufficient supply of iron and some diseases and is therefore not a very reliable indicator.
- *Retinol binding protein* is closely related to prealbumin and can be used as an indicator of changes in the nutritional status (Fidanza, 1991).
- *C-reactive protein (CRP)*, an acute phase reactant, has a close relation with nitrogen balance and catabolic state and can only be used as an indirect indicator of undernutrition. Together with prealbumin, a measurement of CRP can help to determine whether changes in prealbumin are due to cytokine activity or to changes in the nutritional status. A decrease in CRP levels indicates recovery from sepsis and correlates with an increase in the levels of serum proteins.
- *Insulin* like growth factor-1 (IGF-1) level falls with starvation and rises rapidly with refeeding. In addition IGF-1 has a negative predictive value for serious complications in older adults.
- *24-hour urine creatinine* is the most used biochemical index for muscle mass. It has been stated that the creatinine height index is a better indication for undernutrition than weight change, especially in the situation of oedema and obesity. However, 24-hour urine is very difficult to collect in old age and height is another parameter difficult to measure and to interpret (Omran and Salem 2002).
- *Lymphocytes*. The relation between undernutrition and immunologic dysfunction is well known. The effects on T lymphocytes were so far best understood. A decrease in total lymphocyte count (TLC) to less than 800/m^3 reflects severe undernutrition irrespective of age. TLC decreases with progressive undernutrition and correlates with morbidity and mortality (Lesourd *et al.* 1998).

- *Low serum cholesterol levels* have been considered a reflection of low lipoprotein and thus of low visceral protein levels. In nursing homes, lower cholesterol levels correlate with a strong increase in mortality (Rudman *et al.* 1988). However the data on lipids are still controversial, in old age (Simons *et al.* 2001 vs. Lloyd-Jones *et al.* 2003). Even in very functionally impaired nursing home residents, elevated low-density cholesterol is associated with cardiovascular disease. It is assumed that some of the controversy may relate to the increased risk of mortality with low lipid levels in frail older adults. Thus, serum cholesterol in old age is not a very clear indicator of the nutritional status.

8.3.4 Screening tools

Screening tools for undernutrition are compiled from a number of parameters of the nutritional state and are designed for self assessment or must be administered by health care professionals.

- *The Mini Nutritional Assessment* incorporates several domains including functional status, lifestyle, a few questions on diet, subjective health and anthropometric indicators. The sensitivity and specificity of the tool validated against an extensive evaluation by clinicians was respectively 96% and 98%. Biochemical measurements offer no added benefit (Guigoz 2006).
- *The Subjective Global Assessment (SGA)* is designed for clinical use and incorporates functional capacity as an indicator of malnutrition. It relies heavily on physical signs of malnutrition and on malnutrition-inducing conditions. The SGA has a reported sensitivity and specificity of respectively 82% and 72%. Also in this screening tool biochemical indicators have no added value.
- *The Malnutrition Risk Scale* (scales, for sadness, cholesterol, albumin, loss of weight, eating problems, shopping and cooking problems) is a sensitive screening tool, simple to administer and easy to use, especially in an outpatient setting (Omran and Morley 2000). Characteristic in this tool is the inclusion of cholesterol, and emphasis on depression.
- *The MUST (Malnutrition Universal Screening Tool)* includes the BMI, weight loss and some questions on food intake. It is developed for several medical settings and specific for nursing homes. The first signs of evaluation studies are promising.
- *CNAQ (Council of Nutrition Appetite Questionnaire) and SNAQ (Short Nutrition Appetite Questionnaire)* are the first appetite monitoring instruments specifically designed for use among elderly in clinical settings in the USA. The questionnaires consisting of respectively eight and four items have been shown to identify persons at risk of significant weight loss. A validation study indicated that in light of its brevity and comparable reliability, the SNAQ is the more efficient clinical tool (Wilson *et al.* 2005).
- *SNAQ (Short Nutritional Assessment Questionnaire)* a three-item screening tool, includes questions on involuntary weight loss, appetite and the use of

drink or enteral feeding techniques (Kruizenga *et al.* 2005). This screening tool is especially developed for the hospital setting and can be integrated in the nurses' intake at admission to the hospital. This tool approved to be valid to detect malnourished patients at an early stage of the hospitalization.

All the screenings listed have been developed in the past one or two decades and most of them are part of a nutritional care plan in different settings.

8.4 Micronutrient deficiency

Chronic undernutrition will lead to depletion of micronutrient stores, biochemical adaptations/metabolic changes and in the case of very serious shortages to clinical signs. Obviously the method to be applied for the assessment of vitamin deficiency depends on the stage of deficiency and is shown in Table 8.3 (Combs 1992).

Table 8.4 provides an overview of the most common applied biochemical and clinical indicators of deficiencies in selected high risk nutrients. In brief, these nutrients will be discussed below.

- *Vitamin B_6/pyridoxine; folate; vitamin B_{12}/cobalamin.* An inadequate supply of one of these B vitamins causes hyper-homocysteinemia. Homocysteine is prothrombotic and atherogenic and is considered an independent risk indicator of cardiovascular diseases. Prospective studies also suggest a correlation between elevated homocysteine and dementia and oseoporotic fractions (Kalmijn *et al.* 1999, van Meurs *et al.* 2004, and Durga *et al.* 2007). Supplementation with folate and less so with cobalamin or pyridoxine in trials demonstrated a reduction in serum homocysteine. However, up until now trials do not show or are inconclusive in demonstrating a reducing effect on the incidence on cardiovascular disease, dementia or osteoporotic fractures. With the latter outcome measure no trials have yet been published.
- *Vitamin B_6* comprises the various derivates of pyridine, which include pyridoxine, pyridoxal and pyridoxamine. There are many dietary sources and therefore is dietary deficiency rare. Vitamin B_6 deficiency usually occurs in

Table 8.3 Methods of assessment of vitamin deficiency

Stage of deficiency	Most informative method
Depletion of stores	Dietary evaluation Biochemical method
Metabolic changes	Biochemical methods
Clinical defects	Clinical evaluation Anthropometric and biochemical evaluation
Morphological changes	Anthropometric evaluations Clinical evaluation

Table 8.4 Biochemical and clinical indicators in frequently observed micronutrient deficiencies in elderly people

Nutrient	Biochemical indicator	(Sub)Clinical indicator	Range of recommended daily intakes	Main food sources
Vitamin B_6/pyridoxine	• Pyridoxal 5′ phosphate (PLP) in blood/plasma • Erythrocyte aspartate aminotransferase • Homocysteine	• Neuropathy, cheilosis, glossitis, stomatitis • Decreased immunity • Anaemia	1.5–1.8 mg of 0.02 mg/g protein	Many foods, especially meat, fish, also potatoes, vegetables, milk and milk products
Folate	• Serum folates erythrocyte folates • Homocysteine	• Megaloblastic anaemia • Polyneuropathie	200–300 mcg	Vegetables, fruit, whole wheat products
Vitamin B_{12}/ cobalamin	• Serum cobalamin • Methylmalonic acid • Homocysteine	• Megaloblastic anaemia • Peripheral neuropathy • Memory loss, dementia	2.2–5 mcg	Meat, fish, milk products, eggs
Vitamin C/ ascorbic acid	• Serum – vitamin C • Leukocyte vitamin C	• Haemorrhage • Impaired wound healing • Scurvy	70 mg	Potatoes, vegetables and fruit
Vitamin D/calciferol	• Serum 25$(OH)_2$vitamin D_3 • Parathyroid hormone	• Decreased bone density, high fracture risk • Osteomalacia • Diminished muscle condition	10–15 mcg	Fish, meat milk fat
Iron	• Haemoglobin, MCV • Ferritin, transferrin • Serum – iron • Protoporphyrin • Total iron binding capacity	• Always tired, distortions in several organs	11–15 mg	Meat, legumes whole wheat products; small amounts in many foods
Zinc	• Plasma or serum zinc concentrations, leukocyte zinc levels, hair zinc levels	• Impaired immune response, wound healing, vision, taste and smell, confusion, diarrhoea	8–15 mg	Meat, seafood, fresh fruits, vegetables and dairy products

association with other water-soluble vitamins. Deficiency may result from alcoholism, malabsorption and other factors such as dialysis. Medication may act as pyridoxine antagonist.

- *Folate* represents a group of related pterin compounds. More than 35 forms of the vitamin are found naturally. The various dietary sources also include, in addition to plant sources, liver and other organ meats. Folate in foods is destroyed by excessive cooking, as much as 95% may be lost (Stabler and Allen 2004). Studies reveal that folate deficiency may range from 2.5–34% in the elderly. Causal factors in addition to poor intake and absorption are atrophic gastritis, excessive alcohol intake, smoking and use of some drugs.
- *Vitamin B_{12}* is a group of cobalamin compounds with a corrin ring and a cobalt atom in the centre. Vitamin B_{12} is available only from animal foods. The prevalence of deficiency ranges from 4–43%. Van Asselt *et al.* (1998) found in the Dutch SENECA cohort a prevalence of 24%, which could only partly be explained by insufficient dietary intake or atrophic gastritis. The presence of significant vitamin B_{12} deficiency can be confirmed by demonstrating an elevated methylmalonic acid level. Pernicious anaemia, terminal ileal resection, bacterial overgrowth and use of specific drugs are other possible causes for a state of deficiency.
- *Vitamin C/ascorbic acid.* Vitamin C is a water-soluble vitamin widely found in fruits and vegetables. Unfortunately this vitamin is readily lost from foods during storage and preparation. Such losses may account for about 50% of the potential vitamin content in the total diet. It may result in insufficient supply of vitamin C, particularly in older people who make use of catering or restaurant facilities on a daily basis. The reason often being the long journey prepared dishes make from kitchen to consumption. The absorption of the vitamin seems not to be affected by age. Vitamin C deficiency is mainly caused by insufficient dietary intake and the prevalence is most common in frail elderly people. Low vitamin C levels have been associated, in addition to classical deficiency signs, with increased risk of coronary artery disease and senile cataract (Nyyssönen *et al.* 1997, Mares-Pelman *et al.* 2000). The mechanism behind it, is most likely the anti-oxidant properties of vitamin C. For other anti-oxidant vitamins the reader is referred to Chapters 19 and 20.
- *Vitamin D/Calciferol.* Vitamin D refers to a group of lipid-soluble compounds with a four-ringed cholesterol backbone. Vitamin D is not considered as a true vitamin, because the human body can synthesize it with adequate sunlight exposure. In most cultures about one-third of the vitamin D requirements can be obtained from the diet: fish, meat and milk fat. The rest has to be synthesized. As a result of limited sunlight exposure and a four-fold reduced capacity of the skin to produce vitamin D, deficiencies occur especially in homebound elderly people. However, in the relatively healthy older European participants of the SENECA study more than 30% also had low vitamin D levels. Vitamin D supplementation results in decreased bone loss and fracture rate in both older men and women. Recent trials also indicate improvement of sarcopenia and a decrease in falls (Bishoff-Ferrari *et al.*

2005, Jackson *et al.* 2007). It is now accepted that 25(OH) vitamin D levels should be measured in most older persons, and vitamin D replaced in all those with levels below 30 nmol/l.

- *Zinc*. Zinc deficiency is not rare in older persons, particularly amongst diabetics. Zinc is available widely in foods but the bioavailability is better from animal foods than plant foods. In whole grain products phytates may inhibit absorption. Red meat, seafood, fresh fruit and vegetables and dairy products are the main sources. Zinc is involved in protein synthesis, nucleic acid synthesis and gene regulation. Further it is part of several enzymes. Biochemical abnormalities of zinc deficiency include a reduction in plasma zinc concentrations, protein synthesis, activity of metalloproteins, resistance to infection, collagen synthesis and platelet aggregation. Other manifestations of zinc deficiency are anorexia due to impaired taste and smell, impaired vision, confusion and restlessness and sometimes diarrhoea. Zinc measurements are often problematic. Cytokines dramatically reduce serum zinc. Leukocyte zinc levels or zinc hair levels when done properly may be useful.
- *Iron.* Iron has special nutritional interest because of the high incidence of iron deficiency worldwide in the younger age groups. Iron is available in many foods in small amounts, but between foods the bio-availability differs a lot. Two broad categories of iron are present in food: haem iron derived mainly from animal foods and non-haem iron in plant foods. Haem iron is much better absorbed. Because of this difference in biological availability, dietary recommendations vary according to the nature of the diet. These recommendations are difficult to meet in diets with a low bioavailability. However, the requirement is sharply reduced in postmenopausal women and their iron status is correspondingly improved. Adult men generally have no problem in meeting their iron requirement. When anaemia is diagnosed, chronic blood loss or deficiency of folate or vitamin B_{12} should be considered. In elderly using multi-supplements, concern about the iron status should rather be with the avoidance of over-exposure than with the prevention of deficiency (Mertz 1998). To determine iron status, a serum iron, together with a ferriten should be obtained. In some cases measuring soluble transferrin receptors may be useful.

8.5 Treatment of weight loss

When risk for undernutrition or severe weight loss has been diagnosed, a nutritional care plan has to be designed. Non-nutritional cause(s) of weight loss should be identified and treated. The first step in nutritional care is to find the main cause or form of weight loss by asking questions in the following order (Rolland *et al.* 2006):

1. Is weight loss due to dehydration? (Yes/No)
   If not:
2. Is weight loss due to anorexia? (Yes/No)
   If yes, the patient is anorexic:

3. Is weight loss due to anorexia or cachexia? (Yes/No)
   If no, the patient is not anorexic:
4. Is weight loss due to sarcopenia or malabsorption? (Yes/No)

It is possible that weight loss is due to a combination of causes. In such a situation a nutritional care plan should try to treat more then one cause or form of weight loss and if necessary set priorities. Below we discuss the most important features of a nutritional care plan per form of weight loss.

- *Dehydration* requires fluid replacement. Oral replacement is preferred and in most cases sufficient for retaining a normal hydration status. However, the consumption of an adequate amount of drinks should be regularly checked. In clinical settings other devices such as an intravenous catheter can be considered.
- *Anorexia*. Management of weight loss associated with anorexia is focused on stimulating appetite to increase food (energy) intake. There are several ways to stimulate appetite:

  – treatment of potential causes, such as depression;
  – improving meal ambiance;
  – easy excess to snacks and drinks;
  – stimulating exercise.

  Evidence for the effectiveness of a nutritional supplement containing extra energy and protein is limited but indicates some benefit (Milne *et al.* 2005). When they are used, caloric supplements should be given between meals, rather than with meals (Wilson *et al.* 2002). In the latter situation frail elderly may compensate by eating less of the regular meal. This is also shown for so-called 'complete foods', enriched foods with micronutrients added up to the recommended daily intake (Manders 2006). The doses of micronutrients included should not be excessive, since adverse effects of such doses on organ systems have been reported (Palmer *et al.* 2003). Also high doses will affect the taste which makes compliance hard, especially in frail elderly. Anorexic patients often have multiple disorders, and nutritional management should take these disorders into account as well as dietary habits and other environmental factors specific to the patient (Akner and Cederholm 2001). Therefore, a dietitian should be consulted early in the course of weight loss to give a proper dietary advice. Orexenic agents can be applied in patients for whom other approaches have failed. Megestrol acetate and ornithine oxoglutarate prescriptions have shown beneficial effects, but the latter is not available everywhere (Berenstein and Ortz 2005, Morley 2002). A synthetic tetra hydrocannaboid, dronabil, has been shown to increase appetite, but has less effect on weight gain than megestrol (Jatoi *et al.* 2002, Wilson *et al.* 2007). Selective receptor molecules (SARMs), anti-myostatin compounds and ghrelin analogues are in clinical trials.
- *Cachexia*. Rapid loss of weight and severe wasting in cachexia is mainly due to elevated levels of cytokines. These elevated levels are a consequence of

diseases such as cancer, heart-failure, AIDS or other infections. Cytokines directly affect, amongst others, the central nervous system, leading to anorexia, cognitive dysfunction and sickness behaviour. Unlike other causes of weight loss, cachexia is remarkably resistant to hyper energy feeding. Treatment starts with treatment of the underlying disease. Peripheral and parenteral nutrition with simultaneous gastrointestinal feedings can be considered in patients who are acutely ill. Megestrol acetate has been shown to produce weight gain in cachexia. This may occur by suppression of cytokines and the stimulation of central feeding neurotransmitters (Thomas and Vellas 2006).

- *Sarcopenia* in frail elderly people refers to excess loss of muscle mass. Treatment of weight loss should specifically focus on physical exercise including mainly resistance exercises. Further extra energy and adequate protein intake (about 1.5 g/kg body weight) is of importance. Creatine supplements may improve muscle condition. The use of other drugs such as anabolic steroids remains controversial (Morley 2002).
- *Malabsorption.* Normal ageing brings about very few changes that substantially influence digestion of nutrients. If weight loss occurs due to malabsorption, then we deal with pathological gastrointestinal conditions, which should be treated accordingly. Examples in addition to atrophic gastritis are celiac disease and pancreatic insufficiency. Older adults frequently use medication interfering with micronutrient absorption (see Chapter 22), in a nutritional care plan the use of those drugs should be taken into account.

8.6 Ethics

There is a complex ethical question involved in the decision to consider tube feeding in the older demented patient. Overall, available studies suggest that tube feeding does not enhance outcomes (Finucane 2007). On the other hand, for some patients, e.g. those with severe dysphasia following a stroke, tube feeding can be essential to maintain life. The ethical view on tube feeding varies greatly in different countries. In the end, the decision to tube feed depends on the patient's wishes (if an advanced directive or living will is available), or the family member and the health care provider. Families should be aware that there may be harm rather than benefit from tube feeding. On the other hand, there is increasing evidence that aggressive nutritional support by the oral route without a tube may enhance outcomes, making it unethical not to recognize and attempt to treat undernutrition aggressively.

8.7 Conclusions

Undernutrition is the largest nutritional problem faced by older adults. It needs to be recognized early. Its treatment should be aggressive. In particular,

treatment should focus on identifying and treating modifiable causes of weight loss. The use of tube feeding should be limited in dependent persons as its benefit is unclear.

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9

Ageing and changes in body composition: the importance of valid measurements

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The saying 'use it or lose it', definitively applies to muscle in the elderly.

Abstract: The first part of this chapter briefly describes changes in body composition with age, focusing mainly on the elderly. In the second part a description of body composition methodology is given, describing body composition at five different levels (atomic, molecular, cellular, tissue and whole body) and describing a few methodologies that are of special interest in the 'elderly'. Prerequisites for measuring body composition in the elderly are listed and special attention is given to advantages, limitations and pitfalls of often used body composition methodologies in the elderly.

Key words: elderly, body composition, body composition changes, methodologies.

9.1 Introduction

Body composition has long interested mankind. Centuries ago the Greeks dissected human cadavers to get an insight into the structure and build of the body, and drawings from the Middle Ages of gross muscle structure are still famous today, not only from the artistic point of view. With the development of analytical chemistry last century, it was inevitable that this new knowledge would be applied to body tissues, leading to complete human cadavers being analysed chemically. Starting with analysis of foetuses and the cadavers of newborns around 1900 (Camerer and Söldner, 1900), the most important work

of chemical analysis in adult cadavers was performed in the middle of last century (Mitchell *et al.*, 1945; Widdowson *et al.*, 1951). It was found that the variation in chemical composition between individuals was remarkably reduced if data were expressed per unit fat free mass (FFM), and since then FFM (= body weight minus body fat) is generally used to 'standardise' amounts of components in the body. The chemical analysis of human cadavers laid the groundwork for many other, non-invasive (*in vivo*) methods of body composition and today we can tap from a scala of methodologies, ranging from simple body measures as weight and height and skinfold thickness to predict body composition to sophisticated radiological or nuclear methods that actually measure components of body composition (Forbes, 1987; Heymsfield *et al.*, 2005). With the widespread availability of methods and instruments, body composition measurements can easily be incorporated in research or clinic (Jebb and Elia, 1993), but unfortunately not every user is aware of the limitations of the methodologies, sometimes leading to wrong interpretations and conclusions (Deurenberg and Roubenoff, 2002).

From conception to old age, body composition is constantly changing (Forbes, 1987), and it is changing at atomic, molecular, cellular, tissue and whole body level (Wang *et al.*, 1992). It is important to understand those changes at all levels to be able to interpret body composition measurements correctly. Many body composition methods use assumptions to convert the actual body measurement into aspect(s) of body composition. Awareness of these assumptions and their limitations is a 'must' for correct interpretation of results.

There have been a number of recent publications covering body composition in elderly (Baumgartner, 2000; Harris, 2002; Pierson, 2003; Villareal *et al.*, 2005). This chapter will briefly describe the most important changes in body composition with age, especially at old age, and describe a number of often used methodologies to measure these aspects of body composition (or their change) with their advantages and limitations.

9.2 Changes of body composition with age

The chemical body composition of a foetus is characterised by the large fraction of water in the FFM, at about 90 percent at a gestational age of 24 weeks. At birth the amount of total body water (TBW) has decreased to about 80 percent of the FFM and this amount slowly declines further to stabilise at young adulthood at about 73 percent (Forbes, 1987; Heymsfield *et al.*, 2000). Along with the relative decrease in water content, other chemical components obviously increase, and most remarkable is the increase in potassium and nitrogen (muscle) and the increase in calcium and phosphate (bone).

It is not clear whether at older age the hydration level of the fat free mass remains stable. Some studies suggest that it might slightly increase (Heymsfield *et al.*, 1993), but other studies do not confirm this (Visser *et al.*, 1997; Chumlea

et al., 1999). Differences in study populations and methodologies could be a reason, but it is generally difficult to separate age from possible underlying diseases or malnutrition that could be a reason for a disturbed hydration level. However, all data show a much higher variability in TBW content in the elderly, not only between individuals, but also within individuals.

TBW is the sum of intra cellular water (ICW) and extra cellular water (ECW). The newborn has a high ECW/ICW ratio (Forbes, 1987) but this rapidly decreases with age to stabilise at adulthood with males having slightly lower values than females, indicating in fact the higher muscle content in males. As with TBW it is unclear whether the ECW/ICW ratio changes at old age as some studies suggest (Baumgartner 2005). Underlying diseases and malnutrition might be the main reason for a higher ECW content as it is well known that disease and under-nutrition result in relative high ECW levels.

Bone mineral content (BMC) and bone mineral density (BMD) are highly dependent on age (Forbes, 1987). BMD rapidly increases during childhood to reach peak values at the age of about 30 years (Mora and Galsanz, 2003), after which it starts decreasing. This decrease is gradually in males but in females it rapidly accelerates at menopause. Bone mineral content and BMD can be measured very accurately using dual energy absorptiometry (DXA), a technique now available in most hospitals in developed countries.

Skeletal muscle (SM) varies widely between and also within individuals during the life cycle. At adult age it is relatively stable till the age of 40 years, after which it starts to decrease. The decrease seems to be more prominent in males than in females and is also greater in the muscle in the lower body and leg muscle than in the upper body and arm muscle (Janssen *et al.*, 2000). Anthropometry, DXA and MRI allow assessment of regional and total muscle mass (Lukaski, 2005) but nuclear techniques are required for measurement of actual muscle mass (Wang *et al.*, 1996).

Along with a decreased muscle mass with ageing, muscle strength declines. A reduced amount of muscle mass and muscle strength is defined as sarcopenia and has gained interest over recent years as it is associated with impaired thermogenesis, functional disabilities, increased risks for falls and bone fractures and early death. The prevalence of sarcopenia rapidly increases after age 60. Several studies have shown that the combination of sarcopenia and obesity is most strongly related to functional limitations and bears the highest risk for early death in old age (Baumgartner, 2000).

Organ mass (brain, liver, heart, spleen, kidney) increases with age but their percentage of the FFM decreases; first rapidly during growth and stabilising at young adulthood, after which a slower decline sets in at old age, both absolute and relative as fraction of the FFM (Gallagher and Elia, 2005).

Apart from the changes in fat free mass composition, the relative amount of body fat also changes with age. Infants have about 10 to 15 percent body fat at birth, which rapidly increases in the first year of life to subsequently slowly decrease till puberty, in boys slightly more than in girls. At puberty, body fat increases again, notably in girls, but remains more or less stable in boys,

resulting in 'normal' body fat percentages of 10 to 15 percent in adult males and 20 to 25 percent in adult females. There is, however, a large inter-individual variation. During adult life percentage body fat slowly increases, again with a high inter-individual variation, resulting in higher obesity prevalence figures at older age on average. From age 60 onwards body fat starts decreasing, but as weight generally also decreases, percentage body fat can remain high (Forbes, 1987; Seidell and Visscher 2000).

Not only the total amount of fat varies with age, but also fat distribution changes. Subcutaneous fat or fat patterning can be measured with skinfold callipers or from radiographs. In boys, subcutaneous fat increases mainly on the trunk resulting in an android fat patterning, whereas in girls the increases are more prominent in the gluteal femoral region (gynoid fat patterning). This different fat patterning is related to sexual maturity, sex hormone levels and changes in plasma lipid levels.

With the introduction of computer tomography (CT) scanning the importance of internal fat, mainly intra-abdominal fat or visceral adipose tissue (VAT), became clear. Also the amount of VAT changes with age and depends, among other factors, on sex hormone levels. Males generally have more VAT than females and the amount increases with age till about 55 to 60 years. Excess intra-abdominal fat is a risk factor for hyper-lipidemia, hypertension and insulin resistance and diabetes. Women generally have lower amounts of VAT, but at menopause VAT increases rapidly due to the changing hormone levels and with that the risks for metabolic disorders also increase.

The best way to measure VAT is CT or magnetic resonance imaging (MRI), but these methods have an inherent radiation risk (CT) and are expensive (MRI) and therefore they are mainly used in specific research centres and hospitals. Surrogate measures for abdominal fat are waist circumference, waist-hip circumference ratio and sagital diameter (abdominal height). 'Normal values' are used to assess risks, but beware that these values are age, gender and ethnicity dependent.

Another change with age is the increase of intra-muscular fat (Lukaski, 2005). As muscle mass decreases, more and more fat is deposited between the muscle fibres. As a result arm circumferences at old age, for example, do not relate to the same relative amount of muscle tissue compared to younger age, even after correction for subcutaneous adipose tissue.

9.3 Body composition methodology

Body composition can be studied and measured at five different levels: atomic, molecular, cellular, tissue and whole body (Wang *et al.*, 1992). Examples of each level are respectively the amount of body nitrogen, measured by *in vivo* neutron activation analysis; the amount of body water (measured by deuterium oxide dilution); body cell mass, assessed by gamma counting of ^{40}K in the body; adipose tissue, measured by CT or MRI; and whole body fat assessed by

skinfold thickness. It is important to realise that adipose tissue (tissue level) is not the same as body fat (molecular level), and that bone mineral content (molecular level) is not the same as skeletal mass (tissue level).

The five levels of body composition are interrelated and calculations allow measurements at one level to be converted into another level. For example, body nitrogen (atomic level) can be converted into body protein (molecular level) as most nitrogen in the body is found in proteins and the amount of nitrogen in protein is constant at 16 percent. Adipose tissue (tissue level) as measured by CT or MRI can be converted into body fat (molecular level) assuming a constant fat content in adipose tissue of 80 percent. The factors used for those conversions are sometimes component-based (for example, protein contains 16% nitrogen) and thus stable and reliable, sometimes they are derived from experimental observations (property based) and thus prone to – a sometimes considerable – variation.

Various methods are used to measure or to assess the different components of body composition and they can be placed in one of three groups, direct, indirect and double indirect methods (Deurenberg and Roubenoff, 2002). A direct method measures directly the component of interest, for example potassium, nitrogen; and these methods are, apart from a technical measurement error, very reliable. Unfortunately the nuclear methodologies used are not cheap and require technical expertise, hence their use is not very widespread and limited to a few specialised centres.

Indirect methodologies measure body characteristics and use factors to finally calculate the body component of interest. Examples are dilution techniques for body water using deuterium or ^{18}O labelled water or radiation techniques like CT or MRI and dual energy X-ray absorptiometry (DXA). Generally the (property-based) conversion factors used are quite reliable, but they might slightly differ across population groups and differ with age (Baumgartner *et al.*, 1991). The error of indirect methodologies is normally within 2 to 3 percentage points of the body component measured. Indirect methodologies or combinations of indirect methodologies are the method of choice if no direct methods are possible.

Double indirect methods are based on statistical relationships between easy to measure body parameters and the body component of interest. Skinfolds and bioelectrical impedance are examples. The possible errors can be considerable and the validity of the used prediction equations varies heavily across populations and individuals. Using those methods, body composition is not measured but estimated, as the error can be easily as big as five percentage points. Even in epidemiological studies results obtained using these methodologies have to looked upon with some suspicion unless a whole set of criteria is met. This should generally include but is not limited to validation of used prediction formulas in the population assessed. It is always an advantage to measure possible confounding factors as well to be able to explain unexpected outcomes. Playing 'the devil's advocate' pays off in most studies in which double indirect methods are used.

9.4 Body composition measurements in the elderly

When measuring body composition in the elderly there are a number of prerequisites to ensure useable results.

- The method must be convenient, especially for the subjects in the older age range, and the required active cooperation of the subjects or patients should be minimal to ensure valid measurements. For these reasons underwater weighing and to a lesser extent air displacement (BODPOD) cannot be used in elderly people who are not able to cope with the procedures.
- The measurement must be easy to take. For example, stature measurements are affected by kyphosis and even if not, the partial collapse of the vertebra will make height measurements not comparable with measures at younger age and will make interpretations of height-including parameters such as, for example, the body mass index (BMI) difficult. Skinfolds might be difficult to measure as the difference between adipose tissue and muscle is more difficult to palpate in elderly.
- Many methods are affected by changes that might have occurred in body composition. For example, in elderly the distribution of fat over the subcutaneous and internal depots has changed, thus requiring age-specific formulas to calculate body fat from skinfold thickness. Body water distribution has shifted towards extra cellular water, making all bioelectrical impedance formulas based on younger age groups invalid. Body circumference to assess muscle mass (for example, upper arm) are affected by the likely greater intra-muscular fat deposits in the elderly.

All these factors make body composition measurements in the elderly more difficult, not only from the practical point of view but also the interpretation of the data is more difficult and is often prone to error. It should be obvious that the researcher or user in the clinic needs to be aware of the possible limitations and pitfalls of the methods used.

An example of the relative validity of body composition methods in elderly compared to young adults is given in Fig. 9.1. Not only is the inter-individual variation (compared to the reference method) larger in elderly for densitometry, deuterium oxide dilution and DXA, but also the mean values show, although small, a different bias (Bergsma-Kadijk *et al.*, 1996). This different bias becomes a real issue if the body composition data are used for correcting metabolic rate values. Expressed per kg FFM, elderly would have a significantly higher metabolic rate if FFM is obtained by densitometry, but if corrected for FFM obtained by deuterium oxide dilution their metabolic rate would be lower (Table 9.1). More on the issue of metabolic rate in combination with body composition can be found in Gallagher and Elia (2005).

A selection of readily available methods suitable for use in the elderly is described below with specific information about their use and validity in the elderly. These are basically anthropometry, bioelectrical impedance, dilution techniques and DXA. Nuclear techniques, CT and MRI scanning are limited to specialised centres.

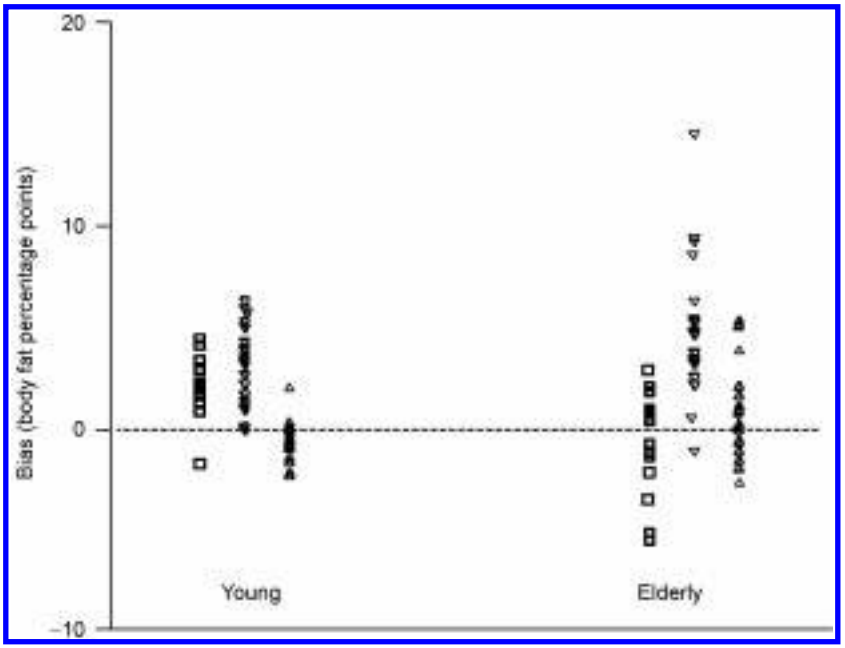

Fig. 9.1 Bias (compared to reference method) in measured body fat percentage using densitometry, deuterium oxide dilution or DXA in 20 young (22 years) and elderly (72 years) females. Reference method was a chemical four-compartment model, measuring body protein by density, total body water by deuterium oxide dilution and total body mineral by DXA (Bergsma-Kadijk *et al.*, 1996).

Table 9.1 Resting metabolic rate (RMR) in young and elderly women expressed per kg fat free mass (FFM), as obtained by different methodologies

RMR/kg FFM (KJ/kg/min) as obtained by:	Young females (n = 20, 22 yrs)		Elderly females (n = 19, 72 yrs)	
Deuterium oxide dilution	0.088	0.008	0.084*	0.005
Densitometry (underwater weighing)	0.084	0.007	0.091*	0.009
DXA	0.084	0.007	0.084	0.004
Chemical 4-C model	0.087	0.007	0.090	0.006

* $p < 0.05$
Bergsma-Kadijk JA, Baumeister B and Deurenberg P, unpublished results

9.4.1 Anthropometry

Body height

Body height is normally an easy to measure parameter, but in the elderly it can be extremely difficult to get the measurement done. There is the problem of the collapse of the vertebra and presence of kyphosis in most elderly, resulting in difficulties standing upright against the measurement board, making adequate

measurements nearly impossible. Unfortunately height is part of the often-used body mass index (BMI, weight/height^2) and is also part of the impedance index (see below). The difficulty of measuring height has resulted in prediction formulas for height, based on, for example, arm span or knee height. Arm span might be difficult to measure in elderly subjects as they might not be able to stretch their arms completely. The usefulness of this measurement can be questioned, because these prediction formulas are developed in a different (usually younger) population with possible systematic bias in the predicted value as the relation between height and the predictive parameter can be different in another cohort. In addition the formulas have a prediction error that is large (3–4 cm). For this reason changes in weight (rather than in BMI) and changes in impedance (rather than using impedance index) are preferable. If standardisation for 'height' is necessary, arm span or knee height could be used instead.

Skinfolds

A reasonably valid method is the measurement of skinfold thickness to assess (subcutaneous) body fat and/or body fat distribution. As subcutaneous fat distribution varies between individuals, it is advisable to measure the thickness of more than just one skinfold to get insight in the amount of subcutaneous fat. Yet often only the thickness of the triceps skinfold is measured. There is a crude relation between subcutaneous fat and total body fat, hence skinfold thickness allows prediction of total body fat (Durnin *et al.*, 1974). The prediction error is, however, considerable and often exceeds 5 percentage points. The prediction formulas are age, gender and ethnicity dependent. Generally, for the same skinfold thickness, women have more total body fat than men and elderly have more total body fat than younger adults. Skinfold measurements *per se* are also useful to follow up without converting the thickness to total fat.

Measuring skinfold thickness reliably requires skills and measurements are more difficult to take in elderly, as it is more difficult to distinguish between fat and muscle tissue. Measurements are also difficult to take in bed-ridden persons. Sometimes skinfold thickness is used in combination with body circumferences to adjust for subcutaneous fat. For example, the upper arm circumference as indicator for upper arm muscle could be biased towards too high values by large amounts of subcutaneous fat.

Waist and hip circumference and sagital diameter

The waist circumference is used as a measure for body fat distribution. It is more difficult to measure in elderly if tissue is loose and landmarks might not be easy to locate. This might not only affect the reading but also the interpretation of the measurement. The same holds for the hip circumference, which used to be used as a reference for waist circumference (waist/hip ratio). The 'normal' values used in adults might not be applicable to elderly and more research has to be done on this point. The sagital diameter (abdominal depths) may be a valid predictor for increased intra-abdominal adipose tissue and associated risks in middle aged but not in elderly.

Arm circumference, calf circumference

The upper arm circumference and sometimes the calf circumference are used as a measure for muscle area (for upper arm and leg respectively). The upper arm circumference has to be corrected for subcutaneous fat tissue, which is normally achieved by taking the triceps skinfold thickness into account (Lukaski, 2005).

With advanced age, fat is deposited between the muscle fibres and this amount cannot be corrected for unless radiographic information (CT, MRI) is available. This makes long-term differences or changes in upper arm muscle area difficult to interpret whereby measurement of the upper arm muscle area is likely to result in an overestimation of muscle mass.

9.4.2 Bioelectrical impedance

In bioelectrical impedance assessment a small alternating current (20 to 100 μA, frequency ranging from 5 kHz to 200 kHz) is applied to the body and conducted by water and dissolved electrolytes in the body. Hence, body resistance or impedance is used as a measure of body water. Total body water (TBW) and extra cellular water (ECW) can be predicted from impedance with empirically derived prediction formulas at high and low frequency respectively. The inclusion of other parameters in the prediction equation such as body weight, age and gender improves the prediction, but this inclusion also makes the prediction less sensitive for changes as differences in impedance reflecting differences in water status might be counteracted by changes in other parameters, mostly weight. For this reason changes in body composition are best observed using impedance values as such.

Most prediction equations are based on statistical relationships between empirically measured impedance index values (height^2/impedance) and body water values obtained by dilution techniques like deuterium oxide dilution and bromide dilution (Visser *et al.*, 1995). Unfortunately the validity of these prediction formulas depends on a variety of factors, among which body water distribution over the extra and intra cellular space (due to differences in specific resistivity) and over the various body parts (due to different shape) is the most important (Deurenberg *et al.*, 1989). As water distribution might be at least more variable (if not different) in elderly, the validity of prediction equations in elderly can be seriously affected and interpretation of impedance values should be made with caution. In many cases it might be wiser to forget about prediction formulas and just interpret changes in term of actual impedance values, preferably segmental impedance values (as of legs, trunk and arms). A decrease in total impedance value above the normal daily fluctuation of about 15 to 20 ohms, may indicate an increase in total body water, or a general shift towards relatively more extra cellular water or a mere re-distribution of water towards the legs (oedema) without much gain in total body water. Figure 9.2 gives data of a person with a normal body water distribution and segmental impedance and body water data (upper part). In the person with oedema (total water gain of 3 kg, see the lower part of figure) and accumulating water only in the legs, total

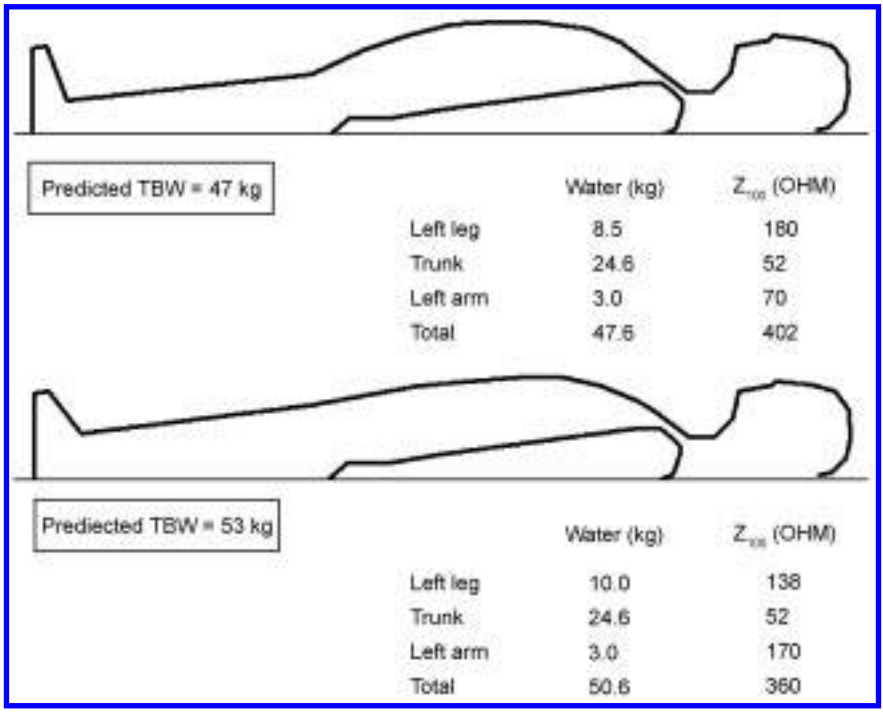

Fig. 9.2 Body water of leg, trunk and arm and their contribution to impedance at 100 kHz.

body impedance decreased with 42 ohms. Using this value in the prediction equation resulted in an overestimation of the change in body water of 3 kg or 100 per cent. This example shows that any abnormality in water distribution, be it geometrically (distribution over trunk and extremities), be it between extra and intra cellular space, has an unexpected effect on (changes in) impedance. The information in Table 9.2 might help interpret (changes in) impedance values.

As body water in healthy subjects is assumed to be a fixed part (73 percent) of the fat free mass (Forbes, 1987), bioelectrical impedance measurements can also be used for the prediction of fat free mass and body fat percent. It should be noted, however, that these predictions might have a relatively low validity and skinfold thickness might be a better tool to get insight in body fatness.

Impedance analysers available on the market vary in their electrical features and in their principles. Many companies developed impedance analysers for the 'big public', anticipating the interest of people in getting information on health and body composition. There are instruments that measure impedance from foot to foot while standing on a weighing scale and consequently provide not only body weight but also body composition parameters. Other instruments measure impedance from hand to hand and allow (with a build-in software program in which weight, height, age and sex has to be entered) the reading of body fat percent. Also combinations of foot-to-foot and hand-to-hand impedance

Table 9.2 Changes in body water compartments and their impact on impedance at low and high frequency and on the impedance ratio

TBW	ECW	ICW	Change in ECW/TBW	Z_l	Z_h	Z_l/Z_h
↓↓	↓↓	↓↓	≈	↑↑	↑↑	≈
↓↓	≈	↓↓	↑↑	≈	↑*	↓*
↓↓	↓↓	≈	↓↓	↑↑	↑↑↑*	↑↑↑*
↑↑	↑↑	↑↑	≈	↓↓	↓↓	≈
↑↑	≈	↑↑	↓↓	≈	↓*	↑*
↑↑	↑↑	≈	↑↑	↓↓	↓↓↓*	↓↓↓*
≈	↑↑	↓↓	↑↑	↓↓	↓*	↓*
≈	↓↓	↑↑	↓↓	↑↑	↑↑↑*	↑↑↑*
≈	≈	≈	≈	≈	≈	≈

TBW: total body water; ECW: extra cellular water; ICW intra cellular water; Z_1, impedance at low frequency, Z_h impedance at high frequency; ↑↑: increase in the parameter; ↓↓: decrease in the parameter; ≈: no change in the parameter; *: relative high or low change due to changes in specific resistively of total body fluid.
Example of how to read the table: An increase in ECW without an increase in ICW will result in an increase in TBW. Impedance at low frequency will decrease and impedance at high frequency will decrease more than expected based on the change in TBW alone as the specific resistivity of TBW decreased. The impedance ratio will also show a higher than expected (based on changes in ECW and TBW) decrease as well.

analysers are marketed. Many of these 'off the shelf' instruments are not suitable for research or use in the clinic, as they do not provide the measured impedance value and the source of the prediction equations is obscure.

9.4.3 Dilution techniques

The use of dilution techniques such as deuterium oxide dilution (or ^{18}O) for total body water and sodium bromide for extra cellular water should not be a problem in elderly people (Visser *et al.*, 1995). The main disadvantages of the techniques and the amount of analytical work and the relatively long time span before the results are available. Also, the use of the methods, namely the analytical part, requires specific skills and hence the methods are not widely used. However, samples can be sent to specialised laboratories to be analysed, which makes the method, in principle, accessible to anyone.

As water content as well as distribution of the water over the two compartments (extra and intra cellular) are important parameters for health and disease (Moore *et al.*, 1963; Heymsfield *et al.*, 2005), their measurement is important. The interpretation is straightforward.

As with bioelectrical impedance, fat free mass can be calculated from total body water, assuming a 73 percent hydration. The errors at both the individual

level and group level are higher in the elderly than in younger adults (see also Fig. 9.1) and interpretation should be done with caution.

9.4.4 Dual energy X-ray absorptiometry

During dual energy X-ray absorptiometry (DXA or DEXA) the body or part of the body is scanned with X-rays of two distinct levels of energy. The attenuation of these X-ray beams by the tissues (fat, lean soft-tissue, and bone) at the two different levels of radiation depends on the chemical composition of each tissue, and is detected by photocells (Pietrobelli *et al.*, 1996; Lohman and Chen, 2005). Software generates a two-dimensional picture of the body or the body compartment under study.

The software is able to calculate several body components: bone mineral content and bone mineral density, lean tissue and adipose tissue. These calculations are possible for each of the body compartments, e.g. for legs, trunk, spine, femur and arms. The method, however, cannot distinguish between subcutaneous adipose tissue and adipose tissue located internally.

The reproducibility of DXA is very high, varying from about 0.5% for bone mineral density to about 2% for total body composition. However, the error is greater for FFM (about 3%) and even greater for (regional) body fat mass (5–10%). The method is quick and easy to perform and requires hardly any cooperation of the subject. The radiation dose (0.02 mSv) is only a fraction of the radiation dose of a normal chest X-ray, and hardly higher than the normal background and if not frequently repeated, scanning should not be a limiting factor. A disadvantage of the method is that the attenuation of the X-rays depends on the thickness of the tissue. Therefore, correction for body size must be made. Compared to traditional methods, DXA scanning is easy and widely available. However, DXA is not free from assumptions and there are many publications showing that the error in measured body composition using DXA can be considerable (see also Fig. 9.1). Also, different machines even when from the same manufacturer and using the same software versions, can give (slightly) different results while scanning the same person.

For the measurement of bone mineral content DXA is the method of choice. The reproducibility and validity is good and the error is small. DXA is also used for the assessment of appendicular muscle mass (Wang *et al.*, 1996; Lukaski, 2005). As there are several assumptions in the derivation of the lean mass using DXA (constant water content of the fat free mass, tissue depths), errors are possible but are generally small.

For the measurement of body fat, DXA might be the most convenient method in elderly as little active cooperation of the subject is required and results are available within minutes. DXA provides no information about body fat distribution and additional measurements have to be taken, either by anthropometry or radiology (MRI) to get that information.

9.5 Future trends

In a well-equipped body composition laboratory, measuring various aspects of body composition is not a problem anymore. However, in the clinical or field situations, especially in sick persons or in the elderly, getting the required information is more challenging. Not only do many assumptions used in healthy adults have at least questionable validity, but also practical problems could create barriers. For that, the development and validation of bedside techniques is important and, for example, validation of bioelectrical impedance should have a high priority as impedance can provide information about the hydration status. This validation should go beyond prediction formulas. Information as provided in Table 9.2 could be of utmost importance, especially when segmental impedance measurements are used. In that way impedance might be a practical tool in the diagnosis and follow up in sarcopenic elderly.

There might be situations where the measurement of body composition is difficult or impossible, and functional measurement (like, for example, muscle strength) might be able to provide the information that is needed. As with body composition techniques, those measurements should be standardised.

Modern techniques like MRI and ultra sound can give more insight into (changes in) body composition with age, and work as done, for example, by the group of Gallagher (1998) will give more insight in the changes of body composition with age in relation to metabolic rate.

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10

Interaction between diet and physical activity in older people

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Abstract: In this chapter the important and beneficient role of exercise for the aging process will be reviewed and the relationship between physical activity and aging will be discussed. An overview is given of the valid and reproducible methods of physical activity measurements in elderly. Scientific and evidence-based physical activity guidelines will be given for elderly people to stay healthy and independent.

Keywords: rate of living theory, energy expenditure, physical activity measurements, energy balance, recommendations for physical activity in elderly people.

10.1 Introduction

Aging coincides with changes in important lifestyles. After retirement, people stop with daily commuting to and from work and although most elderly have ample free time for gardening and sports, their habitual physical activity is declining. Also food habits may change: preparation at home and getting out for dinner. All these changes have consequences for the energy balance.

10.2 Rate of living and energy expenditure

Although vigorous exercise nowadays is being encouraged as an important component of a health maintenance program, this was not the case slightly more than 50 years ago. Even more, in the recent past it was accepted that elderly people should no longer participate in sport and exercise; a lower amount and

frequency of daily physical activity was believed to coincide with aging. This negative attitude towards exercise was largely a consequence of the rate of living theory formulated by Pearl (1928) and was based primarily on the work of Rubner (1908). According to this theory, the greater the rate of energy expenditure and oxygen utilization, the shorter the life span (Sacher, 1979). Subsequently, the stress hypothesis of Sellye and Prioreschi (1960) had a further negative influence regarding the effects of exercise, stating that vigorous exercise represents a stress with long-term harmful effects similar to those of infections, trauma and nervous tension. In addition, the observations that males have a shorter life expectancy than females, whereas males are generally more physically active than females (Kemper and Binkhorst, 1993) and that houseflies live longer the less energy they spend (Sohal and Buchan, 1981) seemed to support the rate of living theory. However, these observations might be confounded by many factors, including energy intake.

Currently, these hypotheses are not generally considered relevant for the long-term effects of strenuous exercise performed regularly. No evidence has accumulated to support the concept that increasing daily energy expenditure by daily physical activity causes the human body to 'wear out' more rapidly or shortens the life span (Holloszy, 1983). On the contrary, it now seems to be well established that cells, tissues and organs of humans develop an adaptive increase in functional capacity and power in response to increased use, which runs counter to the deleterious changes that occur with age. While there is now much supportive evidence for the concept that 'if you do not use it, you will lose it', it does not necessarily follow that strenuous exercise has an effect on the aging process itself (Drenowski and Evans, 2001).

Information regarding the effect of aging on the exercise process is difficult to obtain, particularly in humans. Fitness and sports training programs attract a highly select population: whereas in younger adults 50% of a population may agree to participate, in middle and old age, the proportions of volunteers can be as low as 10% (Shephard, 1978). Slingerland *et al.* (2007) confirmed this trend. They followed respondents aged 40-65 years for 13 years and showed that those retired (n = 684) versus those still employed (n = 287) had a reduction from work-related transportation activities, which was not compensated with an increase in sports participation or in non-sports leisure-time physical activity. One of the most obvious manifestations of human aging is a decline in the ability to exercise and a failure to return to normal levels of functioning as quickly as the young (MacHeath, 1984; McMurdo 2007).

The reduction in adaptability in general physiological functions in our modern industrialized world is illustrated in Fig. 10.1.

After a continuous increase in general physical performance during the growth and young adult period, a gradual decrease of one percent per year is followed till death. The two lines indicate the difference between sedentary and physically active subjects.

Whether regular exercise affects the aging process in humans is extremely difficult to prove because humans are a long-lived species with large genetically

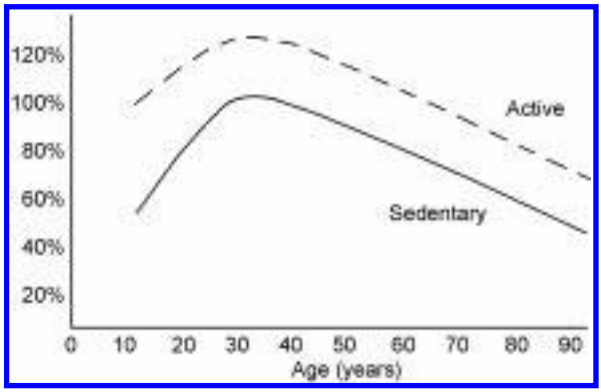

Fig. 10.1 Aging trend in physiologic functions: the relation of physiological functions (%) over age (years) in a general population: the solid line represents the change in sedentary humans and the interrupted line is the hypothesized one for long life physically active humans (with permission, after Smith and Serfass, 1981).

determined interindividual differences in longevity. Moreover, it is not possible to control for a wide range of dietary and other environmental factors that may affect longevity in a freely living aging population (Skinner *et al.*, 1982) though prospective studies start to uncover their impact in the older population segment (Knoops *et al.*, 2004; Sundquist *et al.*, 2004).

10.3 Physical inactivity as a risk factor for chronic degenerative diseases

Physical inactivity is an important direct and indirect risk factor for adult chronic diseases such as cardiovascular diseases, cancer, diabetes mellitus, obesity and other chronic degenerative diseases.

Powell *et al.* (1987) and Berlin and Colditz (1990) have summarized the epidemiological evidence for an indirect and direct causal relationship between physical activity and morbidity and mortality of cardiovascular diseases (CHD). More reviews and a meta analysis come from Blair *et al.* (2001) and Telford (2007). They all come to the conclusion that, although many industrialized countries have adopted prevention policies designed to reduce the prevalence of the three risk factors: high serum cholesterol, smoking, and high blood pressure, physical inactivity should be added as a fourth important risk factor for coronary heart disease (Iestra *et al.*, 2005). A recent review from Hollmann *et al.* (2007) summarized effects of physical activity for health and performance during aging and stated that aging is unavoidable, yet one can counteract its effects into old age even on enhanced cognitive performance capabilities.

Several large-scale epidemiological studies indicate that physical inactivity results in CHD indirectly through various physiologic mechanisms that relate partly to beneficial effects of physical activities on blood pressure and serum

lipoprotein profiles (Powell *et al.*, 1987; Berlin and Colditz, 1990; Murphy *et al.*, 2007). Most studies that have statistically adjusted for the confounding effects of traditional risk factors indicate that physical inactivity is also an independent and direct risk factor for CHD (Powell *et al.*, 1987; Williams *et al.*, 2007). Technological progress in industrialized countries has led to decreasing physical activity in most jobs. Therefore, public health attention is often focused on leisure-time physical activity. The high prevalence of physical inactivity compared to the other three traditional risk factors in the United States is striking. Caspersen (1989), for example, estimated that 59% of the population fails to perform regular leisure-time physical activity. Overall, the prevalence of no leisure-time physical activity peaked in 1989 at approximately 32% and was stable until 1996, after which it declined an average of 1% per year to 25% in 2002. By sex, the prevalence decreased from 29% to 22% among men and from 32% to 28% among women (CDC, 2004). These prevalences are much higher than the 10% of the population with high blood pressure, 10% of the population with hypercholesterolemia, and 18% who smoke cigarettes.

The burden of physical inactivity on public health can be estimated as relative risks for the four selected risk factors. This 'population attributable risk' (PAR) offers a balanced view of the need to act on stronger risk factors that affect fewer people, versus the need to act on weaker risk factors that are far more prevalent. This population attributable risk for physical activity on all causes of mortality and mortality due to CHD seems, in 43 studies reviewed by Paffenbarger and others (Paffenbarger *et al.*, 1986; Blair *et al.*, 2001), greater than the effect of hypertension, hypercholesterolemia, and smoking, mainly because of the large number of physically inactive people. The increase in relative risk (RR) for each of these four CHD risk factors is of a similar magnitude. The RR varies between 1.9 (physical inactivity) and 2.5 (cigarette smoking). With the prevalences of the three other CHD risk factors being relatively low, compared to the prevalence of those failing to perform regular exercise, the PAR of physical inactivity is the highest. Therefore, physical activity in aging people is a greater concern for its population impact than the other three CHD risk factors (Caspersen, 1989; Knoops *et al.*, 2004). Physical inactivity is clearly an important risk factor for CHD.

The mechanization and automation of work and leisure activities have greatly decreased the externally imposed need for physical activity in adults. Physical activity levels are now largely dictated by internal factors, such as body build, physical fitness, and the availability of recreational and sport facilities. Physical inactivity is an important risk factor for many chronic diseases, such as obesity, diabetes mellitus, chronic obstructive pulmonary diseases (COPD), osteoporosis, dementia and CHD. Many researchers have suggested that a sufficient amount and intensity of regular physical activity could decelerate this process (Powell *et al.*, 1987; Nelson, 2007).

Research to document this process longitudinally is largely nonexistent. A few epidemiological prospective studies, comparing physically active people with a randomized group of less-active people over a long period, have been

conducted in the last decade, but apparently cannot be carried out over the whole life-cycle of subjects (Mednick and Baert, 1981).

One of the great concerns is the worldwide scattered increase in overweight and obesity in almost all Western countries in both males and females and also at all ages including the elderly. Nowadays in the US more than 50% of the population is overweight and European countries follow this trend with a delay of about a decennium (See European data WHO 2005, Fact sheet EURO 13/05). Though elderly people are prone to malnutrition, given the high prevalence of physiological, social and psychological risk factors among them, they may also face the consequences of a steep increase in body weight. For malnutrition we refer to Chapter 2. In this chapter we will focus on overweight.

10.4 Energy balance, interaction between diet and activity

Overweight and obesity is a chronic degenerative disease that is probably caused by a long-term positive energy balance. In general from adult age on, body weight remains relatively constant as a result of an energy intake that is on average equal to energy expenditure: the so-called energy balance. However, nowadays in adults total body weight increases gradually by 1 to 2 kg per year. This is the result of a small (not more than 250 kcal/day) but persistent positive energy balance. The difference between daily energy intake and energy expenditure is so small that it can hardly be measured by food intake questionnaires. Also, the yearly increase of body weight by the increase of fat mass is difficult to measure, because a pair of scales at home is not an adequate tool to measure this.

The prevalence of overweight and obesity are particular high in elderly. For instance, in the United States 74% of men and 66% of women aged 60 or older are either overweight or obese, as determined by the BMI (weight in kg/height in m^2). Similar proportions have been observed in Canada and Europe. However, according to an analysis by Janssen and Mark (2007) overweight was not associated with a significantly increased risk of mortality in the elderly while a BMI in the obese range is only associated with a modest increase in mortality risk.

McTigue *et al.* (2006) reviewed articles published between January 1980 and 2005, on the evidence for diagnosis and treatment of obesity in older adults (mean age also > 60 years). They concluded that correlations between body fat and three anthropometric measures (BMI, waist circumference, waist-to-hip ratio) decrease with age but remain clinically significant. Obesity contributes to risk for several cardiovascular endpoints, some cancers and impaired mobility, but protects against hip fracture. They also found that the association between obesity and mortality declines as age increases.

Knowing that a positive energy balance is causing the obesity epidemic, the question is how to stop this or to prevent it. A plausible hypothesis is that the energy balance can only be maintained if energy expenditure is not too low: if

physical activity is too small in a sedentary individual, he/she is at risk for an over-intake of energy. The modern society and the high living standards of the majority of the people make it hard to resist the amount and caloric density of the daily diet. Therefore in the following we postulate that primarily the daily energy expenditure has to be increased and not only the energy intake has to be decreased to balance the daily energy intake over a lifetime period (according Hill's statement: 'food follows activity'). Here we have to add that an increase in physical activity is not only important to prevent obesity, but in old age also essential in the treatment of undernourishment. Physical inactivity triggers a physiological anorexia in older men and women leading to sarcopenia (see Chapter 2).

10.4.1 Human energy expenditure in Paleolithic times

It becomes more and more clear that our present habitual physical activity pattern is the leading cause of the increase in incidence of overweight and obesity. The best estimates about the energy expenditure by our non-overweight Paleolithic ancestors for daily physical exercises amount to about 1000 kcal/day and an energy intake of 3000 kcal/day (Cordain *et al.*, 1998). This results in ratio of 1 to 3. The human living in our modern society has a physical energy expenditure of only 300 kcal/day that goes with an energy intake of 2100 kcal/day, resulting in a ratio of 1 to 7. Eaton and Eaton (2003) suggest that the recommendation of the World Health Organization (WHO), a physical activity level (PAL) of 500 kcal/day, most closely approximates to the Paleolithic standard.

According to the recent excavations in Chad (Africa) the first hominids are almost seven million years old (i.e. a '7' with six zeros). During that extremely long period we were accustomed to a lifestyle characterized by hunting and gathering. This resulted in high daily energy expenditure. In general they were not being richly endowed with food, the energy intake was strongly dependent on availability. Our genes were directed for million years to avoid undernourishment and body weight was always regulated under circumstances with a low energy intake and a high energy expenditure. This kind of physiologic regulation did not lead to an increase in body weight in the majority of the people as today (Fig. 10.2).

The last 70 years, however, the majority of our population experienced the opposite situation: instead of a low energy intake and high energy expenditure, there is high energy intake (overfeeding) accompanied with low energy expenditure (hypokinesia). Because of the low energy expenditure the energy balance becomes positive and leads to an increase in body weight by storage of fat. In this relatively new un-physiologic situation the body weight can only be controlled by cognitive strategies (Dishman *et al.*, 1985). This new concept is illustrated in Fig. 10.3.

To prevent a positive energy balance and an increase of body weight, as in our predecessors was certainly the case; the energy expenditure for physical

Fig. 10.2 Venus of Willendorf: this sculpture of 20,000 years BC shows that in ancient times obesity most likely was not a public health problem, but at least the phenomenon was not unknown.

activities should be increased from 300 to 700 kcal/day. This is more than a two-fold increase. The propagated physical activity norms for health of at least 30 minutes of physical activity with moderate intensity, preferably on all days of the week for elderly (Kemper *et al.*, 2000), are based on the prevention of chronic diseases such as coronary heart diseases (CHD). However, to prevent a gradual increase in body weight occurring over the years, leading to overweight and obesity, probably 45 to 60 minutes of physical activity of moderate intensity is needed. In former obese people that have lost weight by treatment, at least 60 to 90 minutes per day was needed in order to prevent them gaining body weight sooner or later (Saris *et al.*, 2003).

10.4.2 The obesity epidemic

Since the sixties there has been a clear increase in the prevalence of overweight (BMI> 25 kg/m^2) and fatness of obesity (BMI>30 kg/m^2) not only in the US and

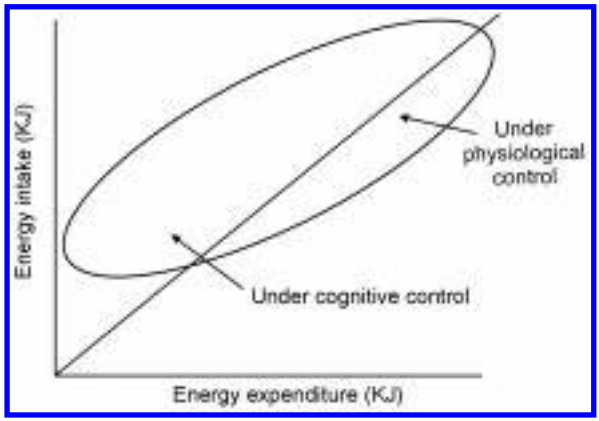

Fig. 10.3 The relationship between energy intake (vertical axis) and energy expenditure (horizontal axis). The diagonal represents the situation in which at any energy level the proportion between energy intake and energy expenditure is one to one: there is energy balance. The ellipse represents the expected individual day-to-day variation in energy intake and energy expenditure: only at a high level of energy expenditure there is balance between both (because of physiologic control). However, at a low level of energy expenditure there is a tendency to a positive energy balance, that is un-physiological and can only be prevented by cognitive control mechanisms (with permission, after Kemper, 2004).

Canada, but also in Europe. In The Netherlands the prevalence of obesity is about 10% for adult men and women. The increase is also discernible in youth (Gezondheidsraad, 2003). In the Survey in Europe on Nutrition and the Elderly, a Concerted Action (SENECA), considerable differences and prevalences of obesity as well as underweight were found across Europe. BMI was above 8–24% of the men and 12–41% of the women (de Groot *et al.*, 2005). There seems to be a clear relation between obesity and other biological risk indicators of cardiovascular diseases such as hypertension, hypercholesterolaemia and type 2 diabetes, but protection for hip fractures during older age. Obesity during childhood and adolescence is supposed to be an important determinant whether a subject will become obese as an adult. It is important to state that overweight and obesity originates in youth and that this an important determinant for adult obesity: it has been found that 40% of the children who were obese at age seven years became obese adults, whereas more than 70% of obese adolescents became obese adults. Apart from genetic and environmental factors lifestyle factors are also associated with the development of obesity in youth; important lifestyles in this respect are physical activity, dietary intake and early events in fetal and infantile growth (Barker, 1998; Vickers *et al.*, 2003).

The epidemic of overweight and obesity has developed in less than three generations in our industrial society and it is not likely that genetics can explain this. More probable is that the energy balance tends to be positive and results in storage of fat mass and a gradual increase of body weight. The average weight increase in adults from age 20 to age 59 years amounts to less than 500 gram per year per person. This is equivalent to an energy remainder of only 10 kcal per

day. This remainder is comparable with less than one cube of sugar 'too much' or several minutes of walking 'too few' per day.

Intensive counseling strategies incorporating behavioral dietary and exercise components promoted a weight loss of 3–4 kg over one to 3.3 years in older individuals. The loss was linked with improved glucose tolerance, improved physical functioning, reduced incidence of diabetes and a combined hypertension and cardiovascular endpoint, and reduced bone density (McTigue *et al.*, 2006). Clearly treatment should include measures to avoid bone loss.

10.5 Measurement methods of physical activity

In order to evaluate the importance of the amount of physical activity for elderly, it is necessary to use measurement methods to assess energy expenditure. However, physical activity of an individual is a behavior that is difficult to measure because most of the time it is subconscious and very complicated (Edholm, 1966; Masironi and Denolin, 1985; Tudor-Locke and Myers, 2001). Job classification, as an important source of physical activity, is not applicable for elderly, because most of them are retired and therefore have no job any more.

10.5.1 Measurements of physical activity and energy expenditure

An important aspect of any assessment of habitual physical activity is the definition and interpretation of the term physical activity. Because the law of the conservation of energy also applies to humans, who must fuel all activity by extracting energy from food, measurements of physical activity are often expressed in terms of energy expenditure (Durnin and Passmore, 1967). Alternatively, physical activity can be expressed as the amount of work performed (watts), as the duration of activity (hours, minutes), as units of movements (counts), or even as a numerical score derived from responses to a questionnaire. Any particular assessment technique, however, measures only one part of so-called 'habitual physical activity' (Montoye *et al.* 1996, Vanhees *et al.*, 2005).

The term energy expenditure is not synonymous with physical activity or exercise. An individual may expend the same amount of energy in a short burst of strenuous exercise (sprint) as in less intense endurance-type activity (walk), but the health and physiological effects of the two could be different.

It is essential to remember that the intake or expenditure of joules is related to body size. A small and lean subject who is very active may spend a similar number of kilojoules in 24 h as a large overweight subject who is sedentary. So, if exercise is expressed as energy expenditure in joules, body size must be taken into account. To this end, energy expended or ingested is sometimes given as kilojoules per unit of body weight or, in the case of oxygen uptake, as millilitres of O_2 per kilogram of body weight. The use of METs (an abbreviation for METabolic equivalent) is another approach to correcting for body weight. A MET-score represents the ratio of energy expended for a specific activity in

kilojoules, divided by resting energy expenditure in kilojoules, either measured or estimated from body size of the individual.

In estimating resting (not basal) energy expenditure, a value of 4.2 kJ per kilogram of body weight per hour or 3.5 ml O_2 utilized per kilogram of body weight per minute is an accepted estimate. A MET-score indicates the energy expenditure of physical activity in multiples of the resting energy expenditure. Also a Physical Activity Ratio (PAR) can be used as measure of energy expenditure of physical activities compared to resting energy expenditure (Westerterp, 2001).

Energy is expended in three ways in warm-blooded humans and animals.

1. A certain amount of energy is required to maintain body temperature and involuntary muscular contraction at rest for functions including circulation, respiration and brain activity. This energy level represents the resting metabolic rate.
2. Some energy is required to digest and assimilate food. This process, referred to as dietary induced thermo genesis or thermic effect of food, adds about 10% to the resting metabolic rate. These two represent in most individuals more than 50% of the total energy expenditure, but can be altered only very slightly in individuals.
3. A third component is the non-exercise activity thermogenesis.
4. By far the most important source of variation between individuals in energy expenditure (when adjusted for body size) is muscular activity. The sources of this activity in elderly are walking, bicycling, gardening (outdoor), housekeeping, stair climbing (at home), and organized sport activities (e.g., golf, tennis, and swimming).

The physiological and biomechanical principles underlying physical activity are complex. Numerous difficulties are encountered in developing simple techniques for assessing habitual activity. For the most part, laboratory methods are not useful in the field for measuring activity and energy expenditure, and do not directly apply to epidemiological studies of assessing habitual physical activity.

The physiologic methods measuring energy expenditure in the laboratory can be divided into three groups:

1. Measurement of energy consumption (food intake), valid only if there is a state of energy balance (i.e., energy intake is equivalent to energy expenditure).
2. Direct measurement of energy expenditure from heat production in a sealed, insulated chamber (so-called direct calorimetry, technically very difficult and not applicable during short term measurements).
3. Indirect measurement of energy expenditure from oxygen consumption in a respiration chamber, or using procedures with 'closed and open circuit' methods using a hood, small face mask, or nose clip and mouthpiece (so-called indirect calorimetry).

The biomechanical methods measure muscular activity by displacement and acceleration of whole body or body segments in two ways:

1. Photographs with high-speed camera or video with subsequent very elaborate analysis, (automatic registration systems and computerized analysis have been recent improvements).
2. Force transducers positioned on the corners of a force plate.

Laboratory methods for measuring human energy expenditure are precise but very restrictive and thus limited to use over a short period of time (Masironi and Denolin, 1985). Field methods are less restrictive and usable over longer periods, but are more imprecise. In the sections below, six different categories of field methods are summarized and evaluated for their usage in measuring in elderly.

The doubly labelled water method

The so-called doubly labelled water method (DLW) bridges the gap between precise laboratory measurements and field measurements (Schoeller, 1983). The method measures integral CO_2 production for up to three weeks from the difference in elimination rates of the stable isotopes deuterium and oxygen-18 from doubly labelled body water after ingestion of a quantity of water enriched with both isotopes. Validation against the precise and near-continuous respiratory gas exchange method, such as in a respiration chamber, has demonstrated that the method is accurate (1–3%), and has a precision of 4–7%, depending on isotope dose, length of elimination period, and frequency of sampling (two-point vs. multipoint). The method is based on a number of assumptions that must be taken into account, depending on the application field. It is assumed that the total body water remains constant, the respiration exchange ratio (RES) equals 0.85 and that there is no exchange of H-2 and oxygen-18 isotopes with non-aqueous body tissue. The DLW method is considered the gold standard for assessing energy expenditure in free living individuals. The method has several advantages over other techniques. It requires only periodic sampling of body fluids; it is non-restrictive, and ideally suited for use with free-living subjects; and, it has the potential to serve as a criterion for validation ('gold standard') of other field methods as mentioned below. However, it gives only overall information of the physical activity pattern and not about time spent on different physical activities.

Observational methods

Assessing physical activity by observation works particularly well when most other assessment methods are unsuitable. Observation, for instance by anthropological methods or video registration, is, however, time-consuming and expensive, and thus not suitable for use in even moderately large groups. In addition, observations are time limited, and may not reflect habitual physical activity. With training, observers can be quite accurate. Various forms are available to make recording more efficient. Also, devices are available, some of

them computer compatible, that facilitate the observation approach of assessing physical activity (Van der Beek *et al.*, 1992, Vanhees *et al.*, 2005).

The diary method

The diary method requires complete cooperation and precision from the subject, so the technique is practical with some populations, such as elderly. In some instances, it is not reasonable to expect subjects to interrupt their daily activities to record physical activity. Data collection is inexpensive, because many subjects can be keeping diaries simultaneously and an observer is not required. The method may interfere with usual behavior and is subject to considerable individual error, although the accuracy is sufficient for group estimates (Bouchard *et al.*, 1983).

Questionnaires and interviews

Although the validity and test-retest reproducibility of questionnaires/interviews concerning physical activity have not been adequately studied, much useful information can be obtained by their use (Reiff *et al.*, 1967; Pols *et al.*, 1990). The use of questionnaires is the only feasible method for epidemiological investigations. Despite the limitations of the method, the results are often correlated with longevity and morbidity. Before selecting a particular questionnaire/interview, it is necessary to define the purposes of the study, time and financial constraints, and the sex, age, and socio-economic characteristics of the population.

The questionnaire method will probably not provide accurate measures of energy expenditure, but it should be possible to group people into three to five categories on the basis of habitual physical activity. Strenuous physical activity appears to be recalled with greater accuracy than mild to moderate activity, and recall of recent activities is more accurate than those done at an earlier time. Weekends and weekdays should be assessed, as well as seasonal variations.

Because most energy-cost-tables of physical activity are based on adult data, substantial errors in estimating energy cost are likely if these tables are used with the elderly (Montoye *et al.*, 1996). The use of METs or PAL minimizes this error (Washburn and Montoye, 1986a).

Motion-sensing devices

Pedometers or step counters are inexpensive, and the most simple type of motion-sensing devices that can be used to estimate habitual physical activity over a relatively long period without interfering with, or requiring modifications of subjects' normal lifestyles (Stunkard, 1960; Le Masurier and Tudor-Locke, 2003). The measurement principle is based on counting the number of steps taken during locomotion with the pedometer fixed around the waist. Steps are counted in response to vertical acceleration of the body, which in the modern electronic devices causes a hammer to hit a sensor, which activates the counter. In the older mechanical devices a lever arm moves vertically and causes a ratchet to rotate (see Fig 10.4a). In the modern ones the vertical acceleration can

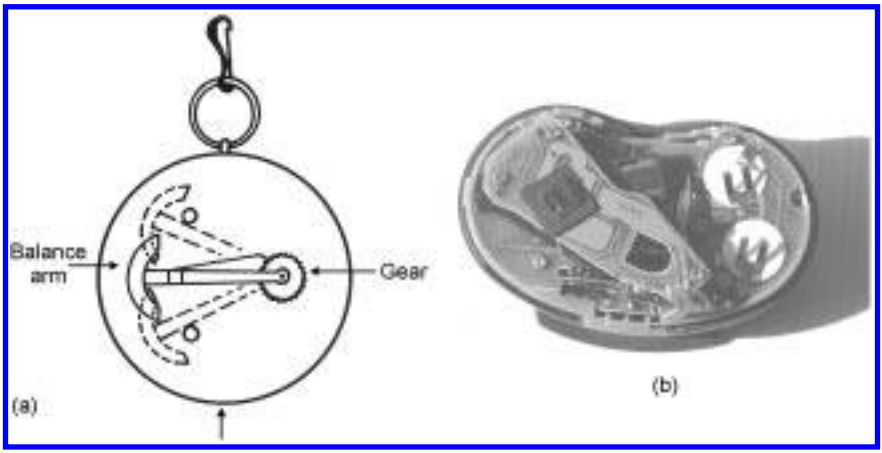

Fig. 10.4 (a) Principle of a mechanical pedometer: when this instrument is attached to the body (arm, leg or waist) a vertical movement causes the lever arm to move up and down and rotates the gear in order to count the numbers (with permission, after Kemper and Verschuur, 1977); (b) A modern version.

be measured electronically (see Fig. 10.4b). From these devices the distance walked or even the amount of kcal expended can be calculated. For the latter calculation a specific MET-score or PAR value for walking should be assumed. There are, however, serious problems with reliability and validity. Currently available pedometers vary in sensitivities, hence, in deviations from the actual step rate, even among those of the same type. The following recommendations have been made regarding the use of pedometers.

- Mechanical pedometers can be calibrated by adjusting the tension of the spring, and thereafter validating the pedometer score against the actual step rate at different walking and running speeds (Kemper and Verschuur, 1977).
- Pedometers offer only a fair estimate of physical activity if most body movements coincide with vertical displacements of the body-centre of gravity, as happens in walking, jumping, running, and stepping. Activities without vertical displacements of the body (such as cycling, skating, and rowing) yield an underestimation of physical activity if the pedometer is utilized.
- Pedometers count the total number of vertical displacements of the body and do not distinguish, for instance, between type of steps caused by a short period of high-intensity running and a long period of low-intensity walking. Because activities of high-intensity require more energy, and are more important for physical fitness and health, in some situations it may be judicious to change the sensitivity so that only activities of a relatively high intensity are measured (for example, running at a speed of 6 km/hr). Moreover, such adjustments prevent registration of passive movements like driving in a car over a bumpy road and other vibration artefacts that are not caused by physical activities (Verschuur and Kemper, 1980).
- Pedometers can also be fixed to the lower limbs in case of cycling.

There is a sound theoretical basis for attempting to estimate physical activity or energy expenditure using portable accelerometers. Pedometers only register displacement but not acceleration of the displacement. Energy expenditure is more proportional to acceleration than to displacement.

Portable, single-plane (vertical) and triple-plane accelerometers are designed to estimate physical activity or energy expenditure based on piezo-electric or piezo-resistive properties of the device (Caltrac, Tritrac and CSA). The inter-instrument variability of these instruments is low, and validity is good in walking or running under controlled laboratory conditions. In the field, however, if kilojoules or kilocalories of energy expenditure in usual activity in a particular season are to be estimated, at least three days, including a weekend day, should be averaged. Accelerometry has been used in elderly people to assess physical activity, but the number of studies is scarce (Gerdhem *et al.*, 2008).

Estimation of energy expenditure from physiological functions

A number of physiological functions reflect the rate of energy expenditure, but heart rate (HR) is the most practical response to measure in the field (Åstrand and Rodahl, 1986). There are dependable, self-contained, portable HR recorders available at reasonable cost (Saris *et al.*, 1977; Vanhees *et al.*, 2005).

The Sports Tester – a small transmitter around the chest in combination with a receiver/recorder as a wristwatch – is rated the best. In populations where day-to-day variation has been studied, 4–5 days of recording (including a weekend day) are usually necessary to obtain a HR index that is typical for an individual (Léger and Thivierge, 1988). To interpret HR as an index of physical activity or energy expenditure, it is imperative to employ individual VO_2-HR calibration curves, or to subtract the resting HR from recorded HR. The second method is simpler and probably almost as accurate (Washburn and Montoye, 1986b). Nevertheless, HR is affected by factors other than the intensity of the physical activity, the most significant being emotions, and thus leaves much to be desired as an index of physical activity or energy expenditure. It is probably most useful when other methods are not feasible – in young children, for example – or in combination with another method.

If one is interested in the amount of moderate and intense physical activity, the estimation of energy expenditure above 50% of VO_2max is a reasonable alternative; however, the determination of each individual's VO_2max would be necessary (Saris, 1986).

The use of motion sensors in combination with HR recording seems to be a promising approach. Recently a new device was introduced (St Onge *et al.*, 2007). This device, worn around the upper arm, measures motion acceleration, skin temperature and impedance and seems to be able to rank subjects according their energy expenditure as measured by DBW.

Summary evaluation

Most of the field methods of assessing habitual physical activity (except job classification) are appropriate for elderly people. The validity is only high for

the doubly labelled water method, which is therefore used as the gold standard of physical activity measurement.

The reproducibility of most instruments is fair and acceptable for use in elderly, but most of the methods are prone to affect the physical activity behavior of the elderly involved during the measurement period.

10.6 Future trends

Because physical inactivity has been established to be an independent risk factor for a range of chronic diseases, older adults are particularly at risk when leading a sedentary lifestyle and increased risk for these diseases.

Because dieting is extremely difficult to continue for many years, and sooner or later the individual reaches their former overweight or above, the daily physical activity level has to be increased not only by sports activities but also by daily routines such as: daily shopping, gardening, dancing, walking and bicycling during leisure time. The use of a simple and cheap pedometer (see Fig. 10.4) can also help in stimulating the daily physical activity behavior of elderly people: knowing that a daily amount of 10 000 steps is equivalent to one hour of moderate intensive physical activity or 500 kcal, may make people aware of their physical activity pattern.

When older people become less independent, and the have to be moved to nursing homes, they have to be stimulated by staff and nurses to remain physically active as much as can be: making or assisting in preparation of their own food, going out walking (to the shop or to enjoy nature) or attending gatherings and leisure time activities with other people.

Increasing the habitual physical activity levels of older people has consequences for our obesogenic environment (Swinburn, 2003). The modern city is built to avoid physical activity: the houses have no stairs, only elevators can reach apartments. The public buildings have escalators and communication in and between offices is only by fax, telephone and e-mail. Transportation to work, school and free time is by car. Sometimes no footpaths are available. At home people communicate only with mobile phones with neighbours without any visit and physical contact.

Changing the physical environment by planning shopping centres within walking distance, bicycle pathways for safe transportation and leisure parks within reasonable distance (not more than 5–10 minutes) is an important prerequisite. On the other hand, improving the knowledge of older people about healthy food and drinks (their energy content and their micronutrients content) and the energy content of daily physical activities (1 km of walking is the same energy expenditure as 1 km jogging) is also important.

King (2001) provided an overview of factors associated with physical activity for older adults and also described potentially promising intervention to promote regular physical activity in this growing population segment. Interventions that appear to be particularly promising for older adults are the ones organized by

level of impact from individual (face to face, group instruction and telephone supervision) to interpersonal approaches (such as physician-based Assessment and Counceling for Exercise (PACE)).

In 2003 Conn *et al.* (2003) published an integrative review of physical activity intervention research with aging adults (65+ and older). From the 17 randomized, controlled trials (RCTs), only one study found greater physical activity in control subjects than experimental subjects. Ten of the 17 studies reported greater physical activity by treatment subjects than control subjects. The RCTs were limited to studies to increase endurance (aerobic or cardiovascular fitness) exercise (walking) or overall physical activity. The mixed findings suggest that additional research is necessary. Evidence of the benefits of resistance, coordination and flexibility is accumulating (Mazzeo *et al.*, 1998).

Many changes occur in the brain with advanced aging that result in neurocognitive decline (Spirduso, 1995). These alterations include atrophy of cortical gyri, decreased brain vascularization and reduction in neurotransmitters in the central nervous system (see also Chapter 11). On a behavioural level the deficits are expressed as slower reaction time, degradation of memory and cognitive performance. However, a physically active lifestyle appears to be uniquely associated with special cognitive benefits in older men and women. Recent results from Bixby *et al.* (2007) suggest benefits from physical activity on the executive function of cognitive tests, controlling for important sources of variability such as education and intelligence quotient. Therefore, a physically active lifestyle seems to maintain and enhance specific aspects of cognitive function in elderly, and the benefits seem to increase with more vigorous activity participation.

10.7 Sources of further information and advice

Recent research (Slentz *et al.*, 2004) acknowledges that the body weight of people remains constant when the amount of energy expenditure (walking or jogging) equals an amount of 12 km per week (Fig. 10.5). This equates to six times 30 minutes per week of walking or bicycling. This is close to the new

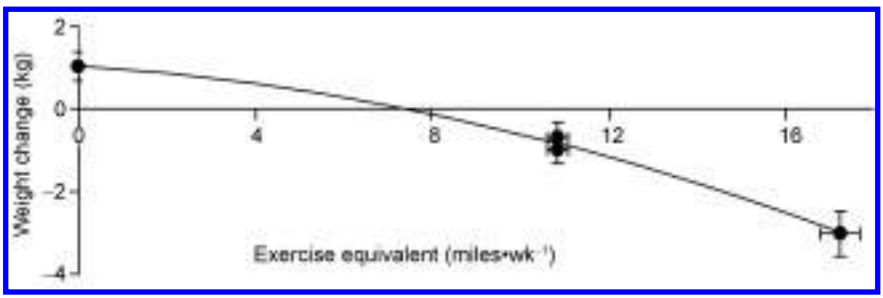

Fig. 10.5 The relationship between weight change (vertical axis) and energy expenditure (weekly covered distance on the horizontal axis): a significant decrease in weight starts when the weekly energy expenditure exceeds a walking distance of more than 8 miles (or 12 km) (with permission, after Slentz *et al.*, 2004).

recommendations given by the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) in 2007 (Nelson *et al.*, 2007):

1. Do moderately intense exercise 30 minutes a day, five days a week or do vigorous intense aerobic exercise 20 minutes a day, three days a week.
2. Do eight to ten strength-training exercises, 10–15 repetitions of each exercise twice to three times per week
3. If you are at risk for falling, perform balance exercises.
4. Have a physical activity plan.

Norms about the minimal amount of daily physical activity have to be given in a format so that people can understand what to do and to check if they reach these norms for being physically active. In the above-mentioned norms of ACSM and AHA moderate-intensity is explained: 'means working hard enough to raise your heart rate and break a sweat, yet still being able to carry on a conversation'. Also the kind of sports activities for older people can be different from younger people (avoiding collision sports, and high impact exercise).

Most important in starting an exercise program for elderly is that they can choose physical activities that appeal to them and make exercise fun.

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11

Prevention of Alzheimer's disease: implication of nutritional factors

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Abstract: Alzheimer's disease (AD) is the most frequent cause of dementia, responsible for 75% of all dementias and it is becoming an increasingly common condition in older people. Environmental risk factors have not been fully identified but nutritional factors have been repeatedly associated with cognitive impairment. Most of this evidence is based on observational studies. A systematic review of the published literature is made in order to identify possible preventive factors for cognitive decline. The review is focused on four major areas of research: antioxidants, B vitamins, alcohol and dietary fats. As available data at the moment do not permit definitive conclusions or specific recommendations regarding diet and AD, all of these dietary components need further enquiry.

Key words: cognitive decline, Alzheimer's disease, nutrition, prevention, older people.

11.1 Introduction

Alzheimer's disease (AD) is an increasingly common condition in older people with a median survival duration from initial diagnosis of 4.2 years for men and 5.7 for women (Larson *et al.*, 2004) and it is responsible for 75% of all dementias. AD is characterised clinically by cognitive impairment, dominated by memory complaints, which may be associated with a syndrome of aphasia, apraxia and agnosia, leading to disorders of executive function and judgement. Furthermore, the natural course of the disease is also associated with a number of specific complications such as behavioural and psychological symptoms (BPSD), weight loss, loss of functional autonomy, enhanced risk of falls and

injuries, which accelerate the process of dependence and the loss of quality of life. Any of these complications can constitute a major burden both to the patient and to the family (Nourhashemi *et al.*, 1997). Even the pattern and rate of cognitive decline in these patients is far from uniform. In clinical practice, certain patients present episodes of rapid cognitive loss (with devastating effects on quality of life), whereas others deteriorate more progressively (Soto *et al.*, 2005).

Data from the Eurostat yearbook 2006/07 show unprecedented demographic changes that will have a major impact on many areas such as social systems or consumption patterns in the coming decades. Increasing life expectancy and reductions in fertility have resulted in the profile of the European Union (EU) population becoming increasingly older. These trends have serious economic and social consequences in a number of areas, including health care and benefit systems. Eurostat's trend scenario for population projections suggests that by 2050 the EU will have 15 million fewer children (aged up to and including 14) compared with 2005, while the numbers of older people will rise. While those aged 55 to 64 will increase by about 4 million, it is with respect to the very elderly that the biggest change will be witnessed, as a total of 51 million citizens are projected to be aged over 80 by 2050 (which is more than twice as many as in 2005). In the same sense, population expected to be over 65 will increase from nearly 17% in the year 2005 to approximately 30% in the year 2050.

Epidemiological studies demonstrate an exponential increase in the prevalence of dementia from age 70 to 94, reaching a plateau at 45% at age 95 and older (Wernicke and Reischies, 1994, Fig. 11.1). Still, there are individuals aged 85 and older with no or just very slight cognitive impairment that are at low risk of developing dementia. These results suggest that while dementia is probably age-related, it is not an inevitable consequence of aging (Panza *et al.*, 2006). As the population is aging and AD is associated with age, the prevalence of AD is expected to quadruple by the year 2047 (Brookmeyer *et al.*, 1998). The same authors conclude that if we could delay the onset of AD for 5 years, we

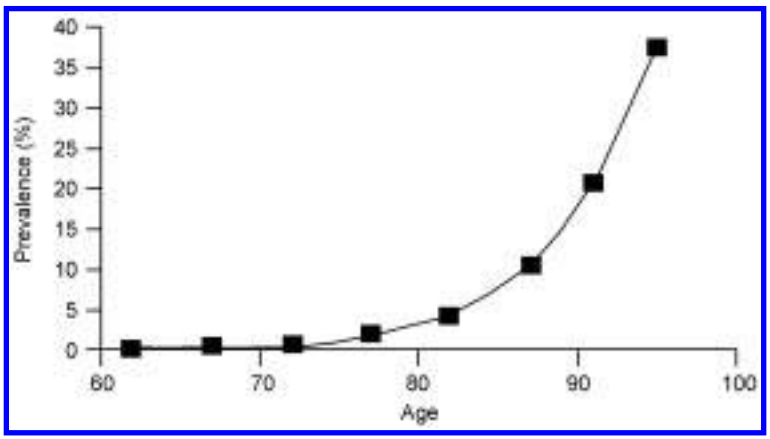

Fig. 11.1 Age-related prevalence of Alzheimer's disease.

would diminish the prevalence by 50%. These data reflect the importance of preventive measures in the field of cognitive decline as at the moment there are no known cures. Taking this into account, the study of the possible role of nutritional factors as preventive factors for cognitive decline is of vital importance.

11.2 Risk factors for Alzheimer's disease (AD)

Although many pathological pathways leading to AD are still unknown, some risk factors have nowadays been identified as having a clear association with cognitive decline. These risk factors include chromosomal mutations, environmental factors and lifestyles. Mutations on chromosome 21, 14, or 1 cause autosomal dominant AD with onset as early as the third decade of life (St George-Hyslop *et al.*, 2000). An allelic variant of apolipoprotein-E, (APOE), ϵ-4, has also been associated with sporadic and familial AD with onset usually after age 65 years (Mayeux *et al.*, 1993). Up to now, the only environmental risk factors identified with the onset of cognitive decline and AD are a history of cardiovascular disease (with its risk factors, hypertension, diabetes and hypercholesterolemia) (Whitner *et al.*, 2005; Dufouil *et al.*, 2005; Zamrini *et al.*, 2004; Piguet *et al.*, 2003; Peila *et al.*, 2002; Knopman *et al.*, 2001; Ott *et al.*, 1999), history of stroke (Honig *et al.*, 2003; Vermeer *et al.*, 2003), and history of atrial fibrillation (De la Torre *et al.*, 2002, Ott *et al.*, 1997).

There is no consistent evidence for nutritional factors to prevent cognitive decline, although observational studies have indicated a relation between particular nutrients and the presence of cognitive impairment and AD. However, cross-sectional studies are useful for hypothesis generation but not for causal inference, as it cannot be established whether AD is a primary or secondary event in relation to diet. On the other hand, the administration of nutrients by supplements does not necessarily have the same impact on the risk of dementia as the dietary intake of the same nutrients. The quality and proportions of the nutrients naturally present in food produce effects on absorption, metabolism and ultimately on bioavailability that are substantially different from the effects that we might expect from the administration of a single nutrient in pharmacological doses (Bronner, 1993). Nevertheless, even with this lack of consistency, nutritional factors play key roles in other diseases, like lifestyle modifications in cardiovascular diseases or the relationship of nutrition and certain types of cancer. Moreover, nutritional factors are key factors in physiopathological pathways of cognitive decline; for example, the associations of APOE gene with lipid metabolism (Saunders *et al.*, 1993). The evidence from observational studies and the evidence in other fields along with the physiopathologic implications make it plausible to continue searching for nutritional factors in the field of primary prevention of AD. Even more, as in cardiovascular diseases, nutrition is a modifiable risk factor with direct implication on the prevalence of the disease.

11.3 Antioxidants

Brain tissue is particularly vulnerable to free-radical damage because of its low level of endogenous antioxidants (Reiter, 1995). Markesbery (1997) proposed an oxidation hypothesis for neuronal death in AD. Vitamin disorders, alteration in metal deposits, beta-amiloid (Aβ) aggregates with a consequent reduction in deposits of iron and copper or an over-production of free radicals lead to oxidative stress when the generation of reactive oxygen species exceeding the capacity of the antioxidant natural defence mechanisms to inactivate them. Oxidative stress has been shown to increase lipid peroxidation, which disrupts the functioning of neuronal cell membranes, and leads to DNA damage, formation of amyloid plaques and vascular lesions type arteriosclerosis with finally neuronal death. The natural defence mechanisms against free radicals include vitamin E (tocopherol), vitamin C (ascorbic acid), carotenes and flavinoids. Vitamin E is a potent antioxidant nutrient that resides within the lipid cell membranes where it neutralises the oxygen free radical molecules as they are generated. Vitamin C, a less potent antioxidant nutrient, circulates within the plasma, and is also known to regenerate the antioxidant capacity of vitamin E.

Several epidemiological studies have indicated a relationship between blood concentrations or nutritional status of antioxidant micronutrients and cognitive impairment. Despite strong evidence of neuroprotection from laboratory and animal studies and moderate evidence of neuroprotection from food sources, the conclusion of absence of protection from vitamin supplements must be drawn.

In the cross-sectional studies (Table 11.1), Goodwin *et al.* (1983) found a correlation between memory test scores and plasma levels of vitamin C in 60 years and older healthy individuals. Schmidt *et al.* (1998) found an association between the concentration of vitamin E and cognitive performance. Perkins (1999) found an association between vitamin E and cognitive decline. On the other hand, Perrig *et al.* (1997) found no correlation with vitamin E but plasma concentrations of vitamin C or carotene were correlated with memory performance and Jama *et al.* (1996) found no correlation at all.

Table 11.1 Cross-sectional studies of antioxidants

		Positive correlation	No/Neg correlation	N
Goodwin *et al.* (1983)	P	Vit C	–	260
Schmidt *et al.* (1998)	P	Vit E	–	1769
Perrig *et al.* (1997)	P	Vit C	Vit E	442
Jama *et al.* (1996)	NE	–	Vit E/Vit C	5182
Perkins *et al.* (1999)	P	Vit E	–	4809
Ortega *et al.* (2002)	NE	Vit E	–	120

P: plasma levels; NE: nutritional evaluation; N: number of participants

Table 11.2 Prospective studies of antioxidants

		Positive correlation	Negative correlation	N Y
Morris *et al.* (2002b)	NE	Vit C and E supplementation correlated with absence of AD		633 4.3 years
Engelhart *et al.* (2002)	NE	Higher intake Vit C and E correlated with lower incident AD		5395 6 years
Luchsinger *et al.* (2003)	NE		Intakes from food or supplements not correlated with AD	980 4 years
Zandi *et al.* (2004)	NE	Vit C and E reduction in prevalence and incidence of AD		4740 3 years
Commenges *et al.* (2000)	NE	Intake of flavinoids protects against AD		1367 5 years

NE: nutritional evaluation; P: plasma levels; N: number of participants; Y: years of follow-up

Regarding the prospective studies, the same inconsistent data have been obtained in four studies (Table 11.2) examining the effect of intake of antioxidant nutrients on dementia. Three of the four studies report statistically significant inverse associations; however, the fourth study by Luschinger *et al.* (2003) found no association after a follow-up of 4 years in 980 patients.

There have been two published randomised trials on vitamin E and Alzheimer's disease. In the most recent trial performed by Petersen *et al.* (2005) supplements of vitamin E (2000 IU/d) had no effect on the progression to Alzheimer's disease among persons with mild cognitive impairment. In an earlier trial by Morris *et al.* (2002a) the same vitamin E dose was significantly related to a combined outcome of time to death, institutionalisation, and loss in physical and cognitive function among Alzheimer's disease patients. However, in the latter study no specific effect on cognitive decline – the central characteristic of AD – was observed.

There are several explanations for the inconsistent findings for food and supplement sources of antioxidant nutrients. First of all, methodological differences in between the studies make generalisations difficult as nutritional status was assessed by different questionnaires (i.e. a 61-item food frequency questionnaire (FFQ), in some of them, which may be less accurate in assessing nutrient intakes than a more articulated FFQ, such as the one used by Morris *et al.* (2002b) (131 items). Additionally, times of follow-up, age of populations, amount of each vitamin supplementation are totally different. Another

explanation could be that dietary intakes of antioxidant nutrients are not related to neuroprotection in humans. This, in turn, may explain, at least in part, the inconsistency between the outcomes of these studies.

Finally, noteworthy is the article published by the Cochrane Hepato-Biliar group (Bjelakovic *et al.*, 2007), a review of randomised controlled trials assessing antioxidant supplements. The conclusions drawn of the Cochrane revision (68 trials including 232 606 participants), established that treatment with beta carotene, vitamin A, and vitamin E may increase mortality and the potential roles of vitamin C and selenium on mortality need further study.

Yet there is strong evidence from animal and laboratory studies to support neuroprotective benefits of dietary components that have antioxidant and anti-inflammatory properties. There have been limited epidemiological studies of the many dietary components with these properties. More prospective epidemiological studies are needed to help elucidate the complex relations of cognitive decline and AD. Further, future clinical trials should be designed to target populations that have low or inadequate dietary intake of the antioxidant nutrients under study. For most nutrients, there might be a range of intake that is optimum for physiologic function, with less than optimum function at both extremes of low intake and high intake. We must not forget to target also potential side effects of high-dose supplementation of antioxidants.

11.4 B Vitamins

Deficiencies of B vitamins, folic acid (B9), and cyanocobalamin (B12), have been associated with cognitive function in many observational studies. More recently, this association has been investigated in relation to hyperhomocysteinemia for which the most common cause is considered to be a deficiency of folic acid or cyanocobalamin (Selhub *et al.*, 2000). Homocysteine is an amino acid entirely derived from the body's intermediary metabolism, which can be converted to either methionine or cysteine. Both folate and cobalamin participate in the methylation of homocysteine to methionine. The other metabolic pathway, which converts homocysteine to cysteine requires the active form of vitamin B6. Homocysteine is active in brain tissue and possibly contributes to the AD pathway through vascular mechanisms or as a neurotoxin (Seshadri *et al.*, 2003). Homocysteine concentration over 14 μmol/L doubled the risk of AD in the Framingham study (Seshandri *et al.*, 2002), but there was no relation of the concentrations of folic acid, vitamin B6, or B12 to the risk of AD.

In addition, vitamin B12 deficiency causes a neurologic syndrome characterised by megaloblastic anaemia, subacute combined degeneration of the spinal cord, peripheral neuropathy, and disturbance in mood and cognition. Irreversible neurologic damage can occur if vitamin B12 deficiency is not treated. Cyanocobalamin deficiency is common in older persons, affecting approximately 20% of those persons 65 years and older (Morris *et al.*, 2002c). There is no neurologic syndrome associated with folate deficiency; however, like vitamin

Table 11.3 Studies of B group vitamins

	Type	Number of patients	Results
Eastley *et al.* (2001)	Prospective	88	No improvement after B12 supplementation
Nilsson *et al.* (2001)	Case series	33 patients suffering from AD	Cognitive improvement with supplementation of B12 and folic acid
Wang *et al.* (2001)	Prospective	370	Low folic acid and B12 levels associated to AD risk
Dufouil *et al.* (2003)	Prospective	1241 4 years follow-up	Circulating levels of homocysteine were inversely associated with cognitive function, independent of B vitamins
Luschinger (2004)	Cohort	679	No association between homocysteine and cognitive decline
Corrada *et al.* (2005)	Longitudinal	579	Low folate intake related with increased risk of AD (not vit C, vit B12 or carotenoid)

B12 deficiency, folate deficiency causes anaemia and neuropsychiatric signs, particularly depression, as reported by Reynolds *et al.* (2002).

There are conflicting epidemiological data on the association of intake and concentration of cyanocobalamin or folic acid with dementia and cognition (Table 11.3). Morris *et al.* (2002c) pointed out in their article the absence of statistical control for dietary confounders as a major limitation of many of the prospective studies of B vitamins that could account for the inconsistent findings. The Chicago Health and Aging Project, CHAP study, controlled for the important dietary and lifestyle variables. Confounding bias is particularly likely for folate intake, as it is associated with many dietary (e.g., antioxidant nutrients, other B vitamins, dietary fats) and other healthy lifestyle variables that have been implicated as protective factors for Alzheimer's disease and cognitive decline. The Cochrane Dementia and Cognitive Improvement group has made a revision on folic acid and vitamin B12 for cognition and dementia in 2003; no conclusions could be drawn on possible benefits after meta-analyses of four randomised controlled trials.

Three double blind, randomised controlled clinical trials, tested the effects of folic acid or vitamin B12 on cognition. The types of study participants were very different in the three trials, which may explain the inconsistent findings. Durga

et al. (2006) found, after three years of treatment, compared with the placebo group, that those receiving folic acid had significantly higher scores on the global combined tests as well as on memory test. The other two studies reported by Eussen *et al.* (2006) and McMahon *et al.* (2006) found no positive benefit on cognition of either treatment of vitamin B12 or vitamin B12 plus folic acid, although the vitamin B12 deficiency was corrected, folic acid increased significantly and homocysteine levels were lowered.

More prospective studies are needed that adequately control for dietary confounders, including vitamin E, niacin, dietary fats, and indicators of vitamin B12 deficiency and more randomised clinical trials of B vitamins and cognition need to be conducted that focus on specific types of patients to determine vitamin supplementation effects in participants who have, for example, deficient levels of the vitamin, normal levels, and high levels. Many vitamin supplement trials have not considered participants' baseline vitamin levels. No evidence-based recommendations can be made on group B vitamin supplementation.

11.5 Alcohol

Alcohol has a paradoxical effect in the brain: on the one hand, lowering the risk of cerebrovascular disease, but, on the other hand, acting as a neurotoxin. Moderate alcohol consumption in human beings is related to greater brain atrophy, but is also related to fewer silent brain infarcts, less white-matter disease and is related to a lower risk of clinical stroke (Mukamal *et al.*, 2001; Sacco *et al.*, 1999). Alcohol consumption increases concentrations of high-density lipoprotein, decreases platelet adhesiveness, and improves endothelial function, which may help to explain the association between moderate alcohol intake and better, well-known, cardiovascular outcomes. Wine contains antioxidants, such as flavonoids, not present in beer and spirits, which may have additional benefits to those of alcohol. Flavonoids can increase membrane fluidity (Halder *et al.*, 1988), antagonise arachidonic acid transport, suppress the 5-lipoxygenase pathway, and subsequently reduce inflammatory responses.

There are several prospective studies that have explored the relation between alcoholic drinks and AD (Table 11.4). As early as 1997, Orgogozo (1997) in the PAQUID study, performed in France, found a relation between intakes of polyphenols (flavonoids) contained in wine and a lower risk of AD in elderly patients. This association was found in moderate alcohol intake but not in the cases of severe intake (more than half a litre of wine a day). Alcohol and wine, in particular, are related to better cardiovascular and cognitive outcomes in observational studies. However, there are no available randomised trials of the effects of alcoholic drinks on these outcomes and no recommendations can be made.

Table 11.4 Studies of alcohol intake and risk of AD

	Type	Number of patients	Results
Galanis *et al.* (2000)	Cohort	3556	Intake of up to one drink a day associated with better cognitive scores than intake of no alcohol; intake of more than four drinks a day associated with cognitive impairment
Truelsen *et al.* (2002)	Case-control	83 incident AD 1626 controls	Intake of wine associated with lower risk of AD. No associations between total alcohol, beer or spirits and risk of dementia
Mukamal *et al.* (2003)	Case-control	373 control 373 AD	1–6 alcoholic drinks per week associated with lower risk of AD
Luchsinger (2004)	Cohort	980	Intake of wine, associated with lower risk of AD, but not total alcohol or other alcoholic drinks

11.6 Dietary fats

Polyunsaturated fatty acids (PUFA) include two major classes: the n-6 or Omega-6 class (e.g., linoleic acid and arachidonic acid), and the n-3 or Omega-3 class (e.g. α-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid). PUFA are a primary component of neuronal membrane phospholipids, and are essential for brain development and functioning (Berr *et al.*, 2006). High levels of DHA are found in the more metabolically active areas of the brain including the cerebral cortex, mitochondria, synaptosomes and synaptic vesicles. Omega-3 PUFAs have anti-inflammatory properties, decrease platelet adhesiveness and diminishes vasoconstriction; while on the other hand, Omega-6 PUFAs enhance trombotic and inflammatory responses (by means of production of prostaglandins and pro-inflammatory cytokines). The same metabolic pathways are used in competition by the two PUFA families. An unbalanced intake of one PUFA in detriment of the other, might favour production of one type of PUFA family instead of the other. High intake of Omega-3 PUFAs from fish or vegetable sources can lower the risk of cardiovascular disease and potentially lower the risk of AD through vascular mechanisms. Several prospective studies have found associations between intake of dietary fats and the risk of AD (Table 11.5), but the mechanisms for these associations are unknown. Fish is the primary dietary source of the longer-chain Omega-3 fatty acids and epidemiologic findings report lower risk of Alzheimer's disease and cognitive decline among fish consumers.

Table 11.5 Studies of fat and fish intake and risk of AD

	Type	Number of patients	Results
Engelhart *et al.* (2002)	Cohort	5395	No associations between fatty acids intake and cognitive decline
Barberger-Gateau *et al.* (2002)	Cohort	1416	Weekly intake of fish associated with low risk of incident AD
Morris *et al.* (2003)	Cohort	815	High intake of n-3 fatty acids and weekly intake of fish associated with lower risk of AD
Luchsinger *et al.* (2002)	Cohort	980	High intake of cal. and fats associated with high risk of AD in Apoe4 subjects

The study findings on fish are generally consistent for a protective association with brain function and disease, yet no randomised controlled clinical trials have been conducted. Because of the likelihood of confounding in epidemiologic studies, randomised clinical trials are required to determine whether the observed protective associations are causal in nature. Furthermore, because of low use of fish oil supplements among older populations, there are no data from epidemiologic studies as to whether fish oil supplements might also be protective. A Cochrane revision made by Lim *et al.* (2006) on Omega-3 fatty acid for prevention of dementia concluded that there is no good evidence to support the use of dietary supplemental Omega-3 PUFA for the prevention of cognitive impairment or dementia.

In summary, there are few and inconsistent studies relating intake of different types of fats and the risk of AD. There are no trial data, and recommendations cannot be made on the basis of these studies. However, a diet low in saturated and trans fatty acids and high in monounsaturated, polyunsaturated and fish-related fats is associated with a low risk of vascular disease and it may be reasonable to extend their benefits to the prevention of cognitive decline and AD.

11.7 Conclusions

Most of the data relating diet and AD are from observational studies and are inconsistent. Thus, recommendations of dietary interventions specifically for the prevention of AD cannot be made currently. However, some of the interventions that are beneficial for other disorders, such as cardiovascular disease, may be beneficial for AD or are unlikely to be harmful and some recommendations could be made.

Randomised, double blind, placebo-controlled trials are needed to assess the potential impact of micro-and macronutrient supplementation and/or dietary

manipulations on the risk of developing cognitive impairment or dementia. Results from intervention trials need to be considered in light of population-based longitudinal studies, because short-term exposure to a dietary or supplemental intake of nutrients is likely to have a different impact from long-standing dietary habits on the risk of developing cognitive impairment.

Interpretation of results and future study designs need to take into account important interactions between diet and lifestyles, physical activity, social and environmental factors, vascular diseases and its risk factors that might act as confounding factors. Even more, the study design will be complex, since exact doses of effective supplementation, the period of life in which the person is most susceptible to AD prevention with supplementation, and the exact duration of supplementation needed to prevent AD, are until now, unknown. Finally, taking into account that AD aetiology is multifactorial, direct nutritional intervention will only have modest results on AD prevention. This results in recruitment of large intervention populations in order to demonstrate a preventive effect of a nutritional intervention.

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Brain lipids and ageing

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Abstract: As lipids account for about half of the brain tissue dry weight, it is not surprising that lipid biochemistry, neurochemistry, membrane structure and function have evolved together with our knowledge of brain function, including studies on ageing.

The lipids in the brain are both a structural component of cell membranes and act as regulators. The amount of lipids in the brain varies spatially, from one region to another, and temporally, with age. The main lipids in the brain are phospholipids, of which phosphatidyl-ethanolamines (including plasmalogens) are the most abundant and are most affected by age. They are followed by phosphatidyl-choline, phosphatidyl-serine and phospho-inositides. Although these last two are the least abundant, they are important in signal transduction. The phosphatidyl-glycerols, mainly cardiolipins, are present in mitochondrial membranes. Sphingolipids (sphingomyelin, cerebrosides, sulfatides) are mainly found in myelin, while others, like gangliosides, are found in all structures. Ceramides could be involved in apoptose during brain ageing. Lastly, there are very few triglycerides in the brain.

Lipids containing long chain fatty acids (and their derivatives) and some essential fatty acids, like ALA, LA and DHA should be part of the diet. Therefore, diet is a key environmental factor that influences the structure and function of the nervous system - and consequently ageing. The fatty acid profile changes with age and each phospholipid in a given tissue (central or peripheral nervous system, retina, white or grey matter), cell, and organelle has a characteristic fatty acid composition. This is particularly so for myelin, which has typically very long chains of saturated, mono-unsaturated and alpha-hydroxylated fatty acids, and nerve-endings (synaptosomes, highly polyunsaturated).

The brain has a very high content of omega-3 polyunsaturated fatty acids and these fats are involved in several neuropsychiatric diseases (depression, Alzheimer's disease) and in the cognitive decline that occurs with age. There is growing evidence from observational, epidemiological, biological and

biochemical studies that omega-3 polyunsaturated fatty acids can protect the brain against ageing and dementia. They may act by protecting neurones, and/or have anti-amyloid, anti-oxidant, anti-inflammatory and anti-atherogenic properties.

As docosahexaenoic acid (DHA) is a primary component of membrane phospholipids in the brain, an adequate omega-3 polyunsaturated fatty acid status is needed to maintain membrane integrity and neurone function; it may also protect against disease.

Most reliable studies have been performed on animals, as the composition of human tissues, including brain lipid and fatty acid composition, may change post-mortem, due to cause of death, duration of any disease, delay before analysis, or temperature.

Key words: alpha linolenic acid (ALA), stearidonic acid (SA), eicosapentaenoic acid (EPA) (also named timnodonic acid), docosahexaenoic acid (DHA) (also named cervonic acid), linoleic acid (LA), arachidonic acid (ARA), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylcholine (PC), phosphatidylinositol (PI), central nervous system (CNS), peripheral nervous system (PNS), blood brain barrier (BBB), cerebrospinal fluid (CSF), Alzheimer's disease (AD).

12.1 Introduction

The brain has a higher lipid content than any other organ in the body, except adipose tissue. Lipids constitute about one half of the brain tissue dry weight. Consequently, it is not surprising that knowledge of brain function, lipid biochemistry, neurochemistry, and membrane structure have all evolved together. The brain contains many complex lipids, some of which were first discovered in the brain, such as phosphoinositides, cerebrosides, sulfatides, gangliosides, and docosahexaenoic acid. Phospholipids account for the very high content of phosphorus in brain. All brain lipids, including most of the phospholipids, are found in cell membranes, and are seldom used as sources of energy. Lipids are efficient repositories of chemical energy (storage fat, primarily triglycerides), but the brain contains virtually no triglycerides.

Most brain glycerolipids are derivatives from phosphatidic acid, diacylated *sn*-glycero-3-phosphate. The fatty acid in the *sn*-1 position is usually saturated, whereas the one at *sn*-2 is unsaturated (except in the retina, where both fatty acids – *sn-1* and *sn-2* – are unsaturated). And the *sn*-1 fatty acid in some glycerolipids is either ether-linked to an aliphatic alcohol (alkyl) or to an alpha-beta-unsaturated ether (alk-1'enyl). The latter lipid is called plasmalogen. Glycerolipids are classified on the basis of the substituent base at the *sn*-3 of the diacylglycerophosphoryl (phosphatidyl) function. The amount of these lipids varies with the brain region and with age. In quantitatively decreasing order in the adult human brain, they are phosphatidylethanolamine (PE), including plasmalogens, phosphatidylcholine (PC), phosphatidylserine (PS). The phosphoinositides are quantitatively minor phospholipids, but they play an important role in signal transduction. The phosphatidylglycerols are present in the

mitochondria membrane in the brain as well as in other tissues. The cardiolopins are the most prevalent phosphatidylglycerols.

Chemically, lipids are compounds containing long chain fatty acids (and their derivatives), or linked isoprenoid units. The fatty acids are either esterified to glycerol (a trihydroxyalcohol), or as amides of sphingosine, a long chain dihydroxyamine (in sphingolipids, the amino group of sphingosine is acylated with long chain fatty acids and the *N*-acylated product is termed a ceramide). The brain also contains a large number of other glycolipids (gangliosides) which are polysaccharide derivatives of glucocerebroside: several monosaccharides, such as galactose, *N*-acetylglucosamine, *N*-acetygalactosamine and fucose are present in various linkages in these carbohydrate head groups. Another important carbohydrate is sialic acid. The isoprenoids are made up of branched chain units and include sterols, such as cholesterol. The brain contains a wide variety of straight monocarboxylic fatty acids, usually with an even number of carbon atom ranging from C12 to C26, saturated, monounsaturated or polyunsaturated. The brain also contains unusual fatty acids, mainly in cerebrosides and sulfatides: odd-numbered and alpha-hydroxylated.

Each phospholipid in a given tissue (central or peripheral nervous system, retina, white or grey matter), cell or organelle has a characteristic fatty acid composition. This is particularly so for myelin and nerve endings (synaptosomes).

Lipids are essential components of plasma membranes and membranes of organelles. They provide the framework for embedded proteins (receptors, enzymes, transporters, ion channels) and function as reservoirs of lipid mediators. There is now evidence that bioactive lipids such as eicosanoids, endocannabinoids and lysophospholipids act as intercellular and intracellular signalling molecules, influencing the physiological and pathological functions of the brain. Membrane-associated processes are important components of metabolism. The acyl composition of membrane bilayers is associated with metabolic activities in a predictable manner in several mechanisms. This has resulted in a proposal that the relative balance between saturated, monounsaturated and long chain polyunsaturated fatty acyl chains in membrane bilayers is a fundamental determinant of most membrane activities. Many membrane-bound proteins (enzymes, transporters, receptors) are affected by alterations in the properties of the lipid bilayer. DHA is an extremely important component of nerve membranes in this respect. A high DHA content is generally associated with high metabolic activity. Highly polyunsaturated acyl chains impart physical properties to membrane bilayers that enhance and speed up the molecular activity of membrane proteins and consequently the metabolic activity of the cells, tissues and whole animals (Hulbert, 2006).

Position 2 of the glycerol molecules in phospholipids generally bears a polyunsaturated fatty acid such as docosahexaenoic acid (DHA; 22:6 (n-3), 22:6ω3), or arachidonic acid (ARA; 20:4(n-6), 20:4ω6). This position 2 may also contain smaller amounts of adrenic acid (22:4ω6) and eicosapentaenoic acid (EPA; 20:5(n-3), 20:5ω3). The brain contains very little alpha linolenic acid (ALA; 18:3(n-3), 18:3ω3), although this is the precursor of all the other omega-3

fatty acids. However, there is very little conversion in humans. Linoleic acid (LA; 18:2(n-6), 18:2ω6), is the precursor of all the other omega-6 fatty acids, mainly as ARA. The omega-3 (ω3), (n-3)) and omega-6 (ω6, (n-6)) fatty acids are essential and strictly complementary, while competing for the desaturases. The human diet usually contains enough omega-6 fatty acids, but insufficient amounts of ALA or DHA. This is why guidelines on dietary lipids and the nervous system focus on omega-3 fatty acids. The nervous system also has high concentrations of saturated and mono-unsaturated fatty acids, but they appear to be endogenous rather than obtained from the diet, with certain possible exceptions.

DHA is the most ubiquitous polyunsaturated fatty acid in nerve tissues, especially in the brain and the retina. It is selectively esterified to amino phospholipids and therefore is prevalent at the cytofacial site of the plasma membrane, where it participates in intracellular events. Representatives of the omega-6 and omega-3 families of amino acids are found in membrane phospholipids, where the omega-6/omega-3 ratio determines membrane fluidity and thus the function of membrane proteins.

The same lipid may act as both a structural and regulatory component of nerve cells. For example, arachidonate is a major constituent of phospholipids, including phosphoinositides. The free acid is also the precursor of a number of important, mainly eicosanoid, messengers (Galli and Petroni, 1990), such as prostaglandins, leukotriens, prostacyclins, and thromboxanes. Lipid signalling includes omega-3 fatty acid derivatives (Chen and Bazan, 2005) that may be involved in the regulation of synaptic function and dysfunction (Bazan, 2005). DHA is the precursor of neuroprotectin, which inhibits oxidative stress mediated pro-inflammatory gene induction and apoptosis, and consequently promotes cell survival. This has been shown in the retina (Bazan, 2006), and could occur in the rest of the nervous system. Arachidonic acid itself also acts as a messenger by activating certain isoforms of protein kinase C, either alone or covalently linked to other groups. For instance, it may form an amide with ethanolamine (amandamide, an endogenous ligand for cannabinoid receptors in the brain). PI (and possibly PC) are intimately involved in signal transduction.

Diacylglycerol is a very important precursor of phospholipid in the endoplasmic reticulum, but it acts as a second messenger in the plasma membrane and activates protein kinase C. Ether lipids, such as platelet activating factors (PAF) are potent messengers. Lipids covalently coupled to proteins have physiological functions (signal transduction, messengers) and also play a major role in anchoring proteins within membranes.

Most lipids are defined by their fatty acid content. Some fatty acids are essential (ALA, LA and DHA), and therefore need to be part of the diet. Thus diet has an important influence on the structure and function of the nervous system. Both macronutrients (Bourre, 2006a) and micronutrients (Bourre, 2006b), together with other food components, alter the predisposition to brain disease or accelerated ageing. Ageing may be speeded up by changes in the vascularisation due to thrombosis or hemostasis. Many studies carried out over

the past 25 years, have documented the impact of nutrition (especially omega-3 fatty acids) in early life on the development of the central nervous system. They have clearly demonstrated that an inadequate supply of those fatty acids has a profound effect on the structural and functional development of the brain (Uauy and Dangour, 2006). Hence, it is not surprising that recent evidence suggests that the omega-3 fatty acid status of older people is associated with brain health.

Several studies on humans and experimental animals have identified the abnormalities of lipid metabolism, particularly phospholipids, that are associated with ageing and a range of neurological and psychological disorders (Bourre, 2004). Most reliable studies have been performed on animals because lifestyle factors and sampling difficulties, such as cause of death, duration of any disease, post-mortem interval, storage time and temperature, all affect the brain lipid and fatty acid composition.

12.2 Main lipids in the brain

The percentage of dry matter in the human brain diminishes continuously between the ages of 60 and 90 years, but the marked differences between individuals suggest that the water content also varies widely. The content of membrane lipids also decreases in parallel, with a marked drop in gangliosides and cerebrosides. These changes indicate a rapid reduction in the amounts of neurone membrane and myelin (Svennerholm *et al.*, 1991).

12.2.1 Glycerophospholipids

The microsomes synthesise less PE and PS with age (Montanini *et al.*, 1983), and the activity of the enzyme phosphatidylserine-decarboxylase decreases, reducing the production of PE (Salvador *et al.*, 2002). The exchanges of choline and serine bases also change during ageing (Ilincheta *et al.*, 2000). Each structure undergoes specific age-induced modifications, especially in the plasmalogens (André *et al.*, 2005).

A lack of dietary ALA results in the selective reduction of PS and an increase in MAO-B activity in the hippocampus of ageing rats, but has no effect on the serotonin and noradrenalin contents (Delion *et al.*, 1997). However, ALA deficiency clearly alters age-related changes in dopaminergic and serotoninergic neurotransmission in the rat frontal cortex (Delion *et al.*, 1996). The turnover of phospholipids (especially PC and PE) and cholesterol in synaptic membranes becomes slower with age (Ando *et al.*, 2002). The lipid composition of the mitochondria in synapses is also affected, especially their LA content (Ruggiero *et al.*, 1992).

12.2.2 Sphingolipids

Ageing induces an increase in both the sphingomyelin content of the rat brain and in its mono-unsaturated/saturated fatty acid ratio (Giusto *et al.*, 2002).

Ceramides mediate the effects of several antagonists leading to cell differentiation, apoptosis and senescence. Ceramide is closely involved in apoptotic cell death in neurodegenerative disorders and ageing. For instance, the concentration of ceramide, perhaps derived from astroglia, in the CSF of Alzheimer patients is increased. This raises the possibility of neurone apoptosis in response to intercellular ceramide in Alzheimer disease (Satoi *et al.*, 2005). Neural sphingomyelinase appears to be the most likely source of senescence-associated ceramide (Venable *et al.*, 2006). The sequence of events in the pathogenesis of Alzheimer's disease may include membrane-associated oxidative stress induced by beta-amyloid, resulting in perturbed ceramide and cholesterol metabolism. These, in turn, may trigger a neurodegenerative cascade that leads to the clinical disease (Cutler *et al.*, 2004).

12.2.3 Gangliosides

The GD1a and GM1 contents of the human frontal cortex decrease more with age than do those of GT1b and GD1b, but there are virtually no changes in individual gangliosides in the visual cortex. The amount of GD1a In the hippocampus is moderately decreased with age, whereas other gangliosides are stable. And the GD1b and GT1b fractions in the cerebellar cortex decrease with age (Kracun *et al.*, 1992). The changes in gangliosides generally differ according to the region of the brain examined and the occurrence of myelin (Ohsawa *et al.*, 1989). The fatty acid content in the ceramide moiety of gangliosides changes with age. For instance, the C20:0 content increases and reaches 27–55% of the total fatty acids (4–9% at birth) (Palestini *et al.*, 1990).

The GM1 monosialogangliosides have neurotrophic activity *in vivo* and *in vitro*. They improve the morphology and biochemistry of cholinergic neurones, and the learning abilities of cognitively impaired aged (and young) rats with cholinergic lesions. They restore the neurochememical, pharmacological, morphological and behavioural parameters in an animal model of Parkinson's disease (Goettl *et al.*, 1999). Lastly, gangliosides are affected in Alzheimer's disease (Kracun *et al.*, 1991).

12.2.4 Cholesterol

Many studies have indicated that cholesterol accumulates in neuronal membranes with age, altering their fluidity, their structure and their signal transduction properties. The increased cholesterol content of cerebral membranes increases the physical rigidity of these membranes and disturbs their function. Membrane fluidity can be restored by a carefully defined dietary supplement of polyunsaturated fatty acids (Yehuda *et al.*, 2002). The optimal ratio between omega-6 fatty acids and omega-3 fatty acids is 5:1. It has been proposed that the uptake of DHA into the brain PE excludes cholesterol from the DHA-rich membrane (Stillwell *et al.*, 2005). In contrast, it is also suggested that the accumulation of cholesterol could help protect neuronal tissue against

oxidative damage (Joseph *et al.*, 1997). Cholesterol deficiency increases the vulnerability of hippocampal glia in primary culture to glutamate-induced exitotoxicity (Chou *et al.*, 2003).

In fact, despite intense research on cholesterol, its metabolism in the central nervous system and its role in neurone development and function are not well understood (Pfrieger, 2003). Studies on animal models have shown that all the cholesterol found in the developing brain is synthesised locally. The cholesterol in myelin is also made locally, and is not imported into the brain (Jurevics and Morell, 1995). Authors postulate that developing neurons reduce their cholesterol synthesis and import cholesterol from astrocytes via lipoproteins. Consequently, neurons use glia-derived cholesterol to form synapses (Claude-pierre and Pfrieger, 2003). Both saturated and unsaturated fatty acids are not only elongated and desaturated during development, but are also used for the *de novo* synthesis of cholesterol (Cunnane *et al.*, 1994; Gozlan-Devillière *et al.*, 1976, 1978; Morand *et al.*, 1979).

Simons *et al.* (2001) have proposed a link between increased serum cholesterol and Alzheimer's disease, but there is some disagreement about the effect of cholesterol during ageing and in relation to dementia. High cholesterol in later life is associated with a decreased risk of dementia, while other observations have shown that high cholesterol in mid-life is a risk factor for later dementia. These conflicting results may be explained by the timing of the cholesterol measurements in relation to the clinical onset of the dementia and to age (Mielke *et al.*, 2005). Clearly, animals fed a cholesterol-enriched diet have altered cognitive functions; spatial learning and the functions of the hippo-campal synapses are altered (Dufour *et al.*, 2006). The statin simvastatin enhances learning and memory independent of amyloid load (Li *et al.*, 2006). Statins also slightly reduced cognitive decline in the elderly, although this relationship is not completely explained by their lowering of serum cholesterol (Bernick *et al.*, 2005).

The precursors of cholesterol are 7-dehydrocholesterol, 7-dehydro-desmosterol, and desmosterol and the cholesterol/7-dehydrocholesterol ratio is an index of PNS development and ageing, but not of CNS development (Bourre *et al.*, 1990a). The precursors of cholesterol are altered in the PNS and CNS of dysmyelinating neurological mutant mice (quaking, shiverer and trembler) (Bourre *et al.* 1989b). Patients with Smith-Lemli-Opitz syndrome are affected by a genetic disorder that results in severe mental retardation; they are unable to convert 7-hydroxycholestrol to cholesterol. Hence, the development such things as learning are sensitive to inhibitors of cholesterol synthesis (O'Brien *et al.*, 2002).

Cholesterol synthesis exceeds the need for structural cholesterol in the adult brain, so that the sterol is constantly excreted from the central nervous system into the plasma at a rate of about 0.023 mg/day (Quan *et al.*, 2003). Curiously, depletion of cholesterol 24-hydroxylase, an enzyme that is very active in the brain, does not alter brain growth or myelination, but reduces sterol excretion from the brain by 64% (Xie *et al.*, 2003). Consequently, there are at least two

pathways of net sterol excretion from the brain. One uses cholesterol-24-hydroxylase and may reflect the sterol turnover in large neurons in the brain. The other probably involves the movement of cholesterol (or one of its metabolites) across the blood brain barrier (BBB), and could reflect sterol turnover in glial cell membranes and myelin (Xie *et al.*, 2003). 24-hydroxycholesterol is an oxysterol formed in the brain that continuously crosses the blood-brain-barrier to reach the blood. There may be an opposite flux of 27-hydroxycholesterol, which is formed to a lesser extent in the brain than in most other organs. 24-hydroxycholesterol is increased, and 27-hydroxycholesterol decreased, in the brain of patients with Alzheimer's disease (Heverin *et al.*, 2004).

Neurosteroids are affected by ageing; they are synthesised in the CNS and the PNS, mainly, but not exclusively, in myelinating glial cells, from cholesterol or steroid precursors imported from other parts of the body. They include pregnenolone (PREG) and dehydroepiandrosterone (DHEA) (Beaulieu, 1998).

12.3 The influence of diet on biochemical changes during ageing

12.3.1 Changes in fatty acid composition

Age-associated changes in the brain content of glycerophopholipids and their fatty acid composition vary from one part of the central nervous system to another (Lopez *et al.*, 1995). A study on the composition of the human cortex of individuals aged from 2 years to 88 years (Carver *et al.*, 2001) found that the concentrations of DHA and of monounsaturated fatty acids increased up to the age of 18. The concentrations of polyunsaturated fatty acids, especially ARA, decreased with age, while that of ALA increased. The polyunsaturated fatty acid content of PE is markedly decreased in Alzheimer's disease (Edlund *et al.*, 1992).

The concentrations of ARA, 22:4ω6 and DHA in the cortex and cerebellum decrease with age, while the concentrations of the 18:1ω9 and 20:1ω9 fatty acids increase (mainly in PE and PS) (Lopez *et al.*, 1995; Giusto *et al.*, 2002). These defects can be corrected by an appropriate diet (McGahon *et al.*, 1999a; 1999b). The age-related changes are associated with altered membrane structures, resulting in reduced cognitive performance, neurotransmission and antioxidant function (Brosche and Platt, 1998). In this respect, the location of DHA, the ALA-deficiency induced DHA depletion and the reversibility of DHA deficiency are specific to certain regions of the brain (Xiao *et al.*, 2005).

The cerebral concentration of the pro-inflammatory cytokine (interleukin-1-beta) increases with age (Martin *et al.*, 2002a), and this may be responsible for the deterioration of certain cell functions, especially as the binding of interleukin-1 to its receptor inhibits the release of glutamate from the hippocampal nerve endings of young rats, but not from those of older rats (Mc Gahon *et al.*, 1998). However, the relationship between changes in brain fatty acid composition with age and diet is poorly documented, even in animals.

12.3.2 Specific alteration in the hippocampus

Ageing results in morphological and neurochemical alterations in brain structures and in their neurones. This is clear for the hippocampus, an important structure of the limbic system involved in memory, which changes with age. The hippocampus undergoes specific changes in its lipid composition and neurotransmitters, often with a transition period between 6 and 12 months (Delion *et al.*, 1997). There are age-dependent modifications in the PE-plasmamogens and PE acyl composition of the hippocampus and the frontal cortex of rats, with a marked reduction in their DHA content that is offset by an increase in monounsaturated fatty acids (18:1ω9 and 20:1ω9). PS is also affected (Favrelière *et al.*, 2000). A diet enriched in DHA (from modified egg yolks or fish) restores the proportions of polyunsaturated fatty acids in PE and PmE, while enhancing the spontaneous and evoked release of acetylcholine (Favrelière *et al.*, 2003).

A diet deficient in ALA leads to a slight increase in the volume of the CA1-CA3 layers of the hippocampus and a decrease in the size of neurones. Magnetic resonance imaging studies on old rats fed an omega-3 deficient diet and rats fed a supplemented diet have shown no difference in the total and regional volumes of gray and white matter (Ahmad *et al.*, 2004). While amounts of DHA (and ARA) are decreased in the hippocampal membranes of aged rats, they can be restored by feeding a suitable diet (Mac Gahon *et al.*, 1999a,b). The age-related impairments of long-term potentiation and depolarisation-induced glutamate transmitter release were reversed by an eight week modified refeeding schedule (Mc Gahon *et al.*, 1999a,b).

12.3.3 Blood brain barrier

The brain needs a continuous supply of nutrients throughout life, but the blood brain barrier (BBB), which determines their supply, is sensitive to ageing (Yehuda *et al.*, 2005). Unfortunately, very little work has been done on ageing and the BBB. A lower concentration of polyunsaturated fatty acids in brain structures could result in poorer movement of solutes across the blood brain barrier, because the enzymes delta-6 and delta-9 desaturase are not adequately incorporated into membranes, or their activities are reduced. These changes, together with an increased production of free radicals due to oxidative stress, can all reduce membrane fluidity (Yehuda *et al.*, 2002).

The fatty acid composition of the brain microvessels also changes with age, and any change in their omega-3 fatty acids produced by an ALA-deficient diet is poorly corrected by changing to an adequate diet (Homayoun *et al.*, 1988). Antioxidant enzymes and related trace elements are altered in the aged brain capillaries and choroïd plexus (Tayarani *et al.*, 1989). A PET study on conscious monkeys showed that DHA improves the age-related impairment of the coupling between neurone activation and the functional cerebral blood flow response, perhaps by modulating cholinergic transmission (Tsukada *et al.*, 2000).

12.3.4 Myelination

Myelination determines the efficiency of the brain and the retina. Nutrition plays an important role in myelination, as myelin membranes are extremely rich in lipids. Severe malnutrition or a lack of essential fatty acids causes severe hypomyelination (Di Biase and Salvati, 1997). Ando *et al.* (2003) have suggested that there is enhanced myelin lipid turnover during senescence.

12.3.5 Peroxisome metabolism

The changes that occur with advancing age are complex in both animals and humans. Omega-3 fatty acids may be directly or indirectly involved, depending on the part of the body, the structure, cells and organelles or lipids concerned (Bourre, 2004). Peroxisome metabolism is also implicated in the control of brain fatty acids during ageing, especially that of polyunsaturated fatty acids (Périchon *et al.*, 1998). Peroxisomes are involved in age-related alterations of membranes: there is a progressive and general decline in peroxisome function during ageing, including a decrease in the fatty acid oxidation pathway that takes place via a specific decrease in acyl-CoA oxidase activity. The age-related decrease in peroxisome function may be linked to a concomitant decrease in cytochrome P450A laurate hydroxylase in the liver (Périchon and Bourre, 1996).

12.3.6 Nerve endings

The compositions of synaptic and nonsynaptic mitochondria undergo different changes during ageing. Among phospholipids, only cardiolipids decrease significantly (26%) in the nonsynaptic mitochondria. The cholesterol (27% decrease) and phospholipid (12% decreased) contents are decreased similarly in the two types of mitochondria (Ruggiero *et al.*, 1992). The incorporation of precursors into the glycerophospholipids of the cerebral cortex and cerebellum also vary differently with age (Ilincheta de Boschero *et al.*, 2000).

12.3.7 Glucose use, lipids and energy in the brain

The concentration of DHA in the brain seems to be an important regulator of its glucose uptake, possibly by affecting the activity of some of the glucose transporters (Freemantle *et al.*, 2006). Older rats also absorb D-glucose less well than young rats, although feeding a diet rich in polyunsaturated fats prevents the age-associated decline in glucose uptake that occurs in rats fed a saturated fat diet (Drozdowski *et al.*, 2003). A reduction in cerebral glucose leads to changes in cerebral metabolism in ageing rats and hence to peroxidation (Benzi *et al.*, 1987).

ALA and EPA may well help to to maintain brain function during ageing not solely by their conversion to DHA, which is very restricted, probably well below 5%. ALA is an efficient ketogenic fatty acid, while EPA promotes fatty acid oxidation. By helping to produce ketone bodies, ALA and EPA could be

contributors to strategies that use ketone bodies to bypass problems caused by impaired glucose access to the brain during ageing (Freemantle *et al.*, 2006).

12.3.8 Red blood cells as marker of brain fatty acid composition

Erythrocytes are good models for brain membranes, and specifically for the relationship between diet and membranes. The amounts of fatty acids in the human cerebral cortex change from early childhood through late adulthood, and the concentrations of several fatty acids in erythrocytes may be useful for predicting the fatty acids in adult brains (Carver *et al.*, 2001). This relationship probably also holds for elderly people. Caprari *et al.* (1999) found that the concentrations of DHA in the PS and PE of centenarians were much better than in the younger controls.

12.4 Relationship between cognitive changes during ageing and lipids

12.4.1 Cognitive changes

A recent French study showed that the age-related cognitive deficit is linked to a reduction in the omega-3:omega-6 fatty acid ratio in erythrocytes (Heude *et al.*, 2003). An excess of nutritional linoleic acid has also been linked to a decline in cognitive performance, while the reverse is true for fish oils (Kalmijn *et al.*, 1997a, b). Fish consumption may be associated with a slower cognitive decline with age: the decline was 10% slower among persons who consumed one fish meal per week than in controls eating no fish, and 13% slower in persons who consumed two or more fish meals per week (Morris *et al.*, 2005). High intakes of mono-unsaturated fatty acids and polyunsaturated fatty acids and total energy are significantly associated with a better cognitive performance, as shown in a 8.5 year follow-up of 95 normal old people aged 65–84 years (Solfrizzi *et al.*, 2006). Thus, a typical Mediterranean diet appears to protect against age-related cognitive decline. Increased oxidative stress during ageing, due to reduced protection against free radicals, can result in a lower omega-3 fatty acid concentration in the nervous system. Hence a diet rich in EPA could have antioxidant properties that help counteract the effects of ageing (Martin *et al.*, 2002b). PC improves the memory, learning, concentration, vocabulary recall and mood in elderly people suffering from cognitive loss (Kidd, 1999). PC, together with vitamin B12, improves learning in the ageing mice (Hung *et al.*, 2001).

There appears to be no question that an adequate intake of omega-3 fatty acids ensures the turnover of cell membranes, so helping to protect the brain against ageing. However, a dietary supplement of high concentrations of omega-3 fatty acids produces behavioural changes that vary with the age of the individual, improving learning in young animals, but reducing learning and motor activity in older ones (Carrie *et al.*, 2000). This should be borne in mind when considering dietary supplements. Studies on patients suffering from

amnesia indicate that ARA + DHA supplementation can disturb the cognitive function due to organic brain damage or ageing (Kotani *et al.*, 2006).

12.4.2 Dementia, lipids and diet

A variety of neurological disorders, including Alzheimer's and Parkinson's diseases, and Huntington's chorea, are associated with a loss of specific populations of neurons. Each of these diseases has a unique constellation of behavioural and neurological abnormalities that result from the loss of neurons in specific regions of the brain (Walsh and Opello, 1992). Attempts to prevent these neurodegenerative diseases have included using dietary polyunsaturated fatty acids, especially for Alzheimer's disease. A mixture of ALA and LA (molar ratio ¼), given in capsules containing vegetable oil, improved the quality of life for people suffering from Alzheimer's disease, as measured by tests of mood, appetite, spatial orientation, cooperation, sleep and hallucinations, and short and long term memory (Yehuda *et al.*, 1996).

Recent ecological and epidemiological studies have shown that dietary EPA and DHA may be important for preventing dementia. The Rotterdam study showed that the risk of dementia (with vascular features) was negatively correlated with the consumption of fish rich in omega-3 fatty acids and positively correlated with the consumption of saturated fatty acids (Kalmijn *et al.*, 1997a). But this result was not confirmed in another study (Engelhart *et al.*, 2002). In the United States, Morris *et al.* (2003a, b) found that a diet rich in unsaturated fatty acids and unhydrogenated fat protected against Alzheimer's disease, unlike a diet rich in saturated fatty acids and *trans* fatty acids. The consumption of meat is poorly correlated with an increased risk of dementia in France, while the consumption of fish has a protective effect. This was found by following participants in the PAQUID study, which lasted seven years and involved 1416 subjects aged over 67 living in the south west of France. The population included 170 cases of dementia, 135 of whom suffered from Alzheimer's disease. Those subjects who ate fish at least once a week were 34% less likely to develop any form of dementia, and 31% less likely to suffer from Alzheimer's disease than those consuming nearly none. The effect was still present when socio-economic factors were taken into account, as these factors are linked to both the reduced risk of Alzheimer's disease and fish consumption (Barberger-Gateau *et al.*, 2002). Similarly, a study carried out in the USA found that Alzheimer's disease was 60% less common in people that consumed about 60mg DHA per day (at least one seafood meal a week) than in people that ate very little (Morris *et al.*, 2003a,b). The findings were similar in Japan (Otsuka, 2000). The Framingham Heart Study suggests that eating 180mg/day or more of dietary DHA (approximately 2.7 fish servings/week) is associated with an approximately 50% reduction in the risk of dementia. At least this amount of DHA is found in one commercially available 1-g fish oil capsule given daily (Johnson and Schaefer, 2006). In contrast, giving patients with mild to moderate Alzheimer's disease 1.7g DHA and 0.6g EPA each day for six months (204

patients, MMSE > 14, age range 74 ± 9 years) did not delay the rate of cognitive decline according to the MMSE or the cognitive disease assessment scale. However, a small group of 32 patients with very mild Alzheimer's disease (MMSE > 27 points) responded positively (Freund-Levi *et al.*, 2006).

A low plasma concentration of omega-3 fatty acids (including DHA) is an indication of the risk of cognitive deficiencies and various types of dementia, including Alzheimer's disease (Conquer *et al.*, 2000). But another study found that plasma omega-3 fatty acid concentrations were unaltered in patients with Alzheimer's disease (Laurin *et al.*, 2003).

Several explanations have been proposed for the way omega-3 fatty acids protect against dementia. As DHA is a primary component of membrane phospholipids in the brain, an adequate omega-3 polyunsaturated fatty acid status may protect against dementia by maintaining membrane integrity and neurone function (Lim *et al.*, 2006). DHA attenuates the secretion of amyloid-beta (Abeta) by human neural cells under cytokine stress, and this effect is accompanied by the formation of NPD1, a novel DHA-derived 10,17S-docosatriene (Lukiw *et al.*, 2005).

A nutrigenomic mechanism might work in conjunction with the other mechanisms, as a diet rich in omega-3 fatty acids can alter the expression of genes in the brain, including those genes involved in controlling synaptic plasticity, cytoskeleton and membrane association, ion channel formation, signal transduction and energy metabolism, and in counteracting the appearance of amyloid aggregates (Ross, 2005). Thus, fish oil consumption might encourage the expression of genes conducive to brain maintenance during ageing. This might be one reason why the fatty acid profile of a subject's erythrocytes was found to be related to cognitive function at the age of 64 (Whalley *et al.*, 2004a,b). However, the available data are insufficient to draw strong definitive conclusions about the effect of omega-3 fatty acids on changes in human cognitive function in normal ageing, or on the incidence, prevention, or treatment of dementia. But there has been no published report on the use of omega-3 fatty acids to prevent dementia.

12.4.3 Vascular dementia and lipids

Vascular dementia and Alzheimer's disease have nutritional factors in common – an excess of omega-6 fatty acids and a lack of omega-3 fatty acids. They lead to changes in the microvasculature, chronic inflammation, platelet aggregation and endothelial dysfunction (Otsuka *et al.*, 2002). These changes provide at least a partial explanation of why the cognitive disorders that occur in very elderly people are positively correlated with the consumption of LA, and negatively correlated with the consumption of fish. The cardiovascular risk increases the risk of dementia, particularly vascular dementia (Kalmijn *et al.*, 2000). Inflammatory processes may well be implicated in all these disorders (Simopoulos, 2002). Nevertheless, the influence of omega-3 fatty acids on vascular components and the cerebral parenchyma is not yet completely clear.

Omega-3 polyunsaturated fatty acids may protect against dementia by reducing cardiovascular disease (Tully *et al.*, 2003) and the risk of non-haemorrhagic stroke (He *et al.*, 2002; Iso *et al.*, 2001). The action of omega-3 polyunsaturated fatty acids in reducing the risk of death from coronary heart disease has been extended to the elderly (Harris, 2003). Conversely, cardiovascular diseases have been shown to increase the risk of dementia, including Alzheimer's disease and vascular dementia (Hofman *et al.*, 1997). Omega-3 fatty acids lower the serum concentrations of triglycerides and blood pressure, and improve endothelium function (Din *et al.*, 2004). Fish consumption is directly correlated with these effects (Friedland, 2003; Issa *et al.*, 2006). A lower omega-6/omega-3 fatty acids ratio may also promote a healthier balance of eicosanoids, which would protect membrane function.

A longitudinal study on the dietary intakes and plasma lipids of healthy elderly men and women showed that the decreases in total fat and cholesterol intakes were significantly correlated with the decrease in total plasma cholesterol (Garry *et al.*, 1992). Although it is particularly important to collect information on the dietary intakes of older adults because of the worldwide phenomenon of population ageing, very little information is available on the changes in dietary intake of non-institutionalised adults over the age of 70. For instance, there is no indication of an age effect on nutrient intakes in New Zealand. However, there are indications that older adults, particularly women, are making changes towards healthier food choices (Fernyhough *et al.*, 1999).

An important tool has been developed in clinical practice for measuring the nutritional status of elderly people: the Mini Nutritional Assessment (MNA) (Vellas *et al.*, 2006, chap. 2.5).

12.4.4 Alcohol and obesity

Curiously, there appear to have been no studies on the implication of omega-3 fatty acids in alcoholism and alcoholic dementia, although animal experiments have shown that dietary ALA modulates the effects of alcohol on various membranes, including nerve endings (Zerouga *et al.*, 1991). There may be a correlation between dementia and overweight. (Gustafon *et al.*, 2003; Gustafon, 2006).

12.5 Lipids and sensory organs

A number of pathophysiological processes underlie age-related changes in the neurosensory systems. The loss of cells can have consequences far beyond the immediate loss of hearing, vision, smell or taste, and may have profound effects on how a person functions. Impairment of these senses, although common, is life threatening, especially when it involves the elderly. Ageing undoubtedly contributes to sensory dysfunction (Boyce and Shone, 2006). This may alter the regulation of energy balance and the control of food intake (Donini *et al.*, 2003, also Chapter 3 by Donini in this book).

12.5.1 Retina, vision and fatty acids

Omega-3 fatty acids have a direct influence on vision as the retina has a very high DHA content (Anderson *et al.*, 1992; Bazan *et al.*, 1994). DHA is concentrated in the specialised membrane that makes up the photoreceptor outer segments. It contributes about 35–65% of the fatty acids in the PE and PS of the outer segment of photoreceptors in species ranging from frogs to humans. DHA occurs almost entirely in the *sn*-2 position of the phospholipids, and it accounts for 75% of the fatty acids in this position in retinal PE. Approximately 60 molecules of phospholipid surround each molecule of visual pigment. Thus, the retinal photoreceptor membrane contains the body's highest concentration of DHA. DHA is extremely important for vision, involving both the brain and the retina, including photoreceptors, neurotransmission, rhodopsin activation, cone and rod development, and the development and maturation of neurones and synapses (Neuringer, 2000; Uauy *et al.*, 2001).

Young rats that lack ALA have an altered fatty acid distribution in the membranes of retina cells, and this changes the amplitude of the 'a' and 'b' peaks of the electroretinogram (Bourre *et al.*, 1989a). The 'a' wave is generated primarily by the photoreceptors, whereas the 'b' wave, a later cornea-positive component, is generated by the inner retina. Injected DHA is actively taken up by the retina (Bazan and Scott, 1990). Supplementing the diet with phospholipids with a high DHA content (together with ARA) improves the visual function of both old mice and young mice lacking omega-3 fatty acids (Carrie *et al.*, 2002). An increase in plasma DHA parallels an increase in DHA in the retina, but the concentration of DHA in the retina remains unchanged when the plasma concentration rises above a given level. Lowering the LA/ALA ratio does not improve visual performance (Jensen *et al.*, 1997), so this ratio alone is not a sufficient definition.

Age-related macular degeneration (AMD) is a major cause of disability in the elderly. Low dietary intakes and plasma concentrations of n-3 fatty acids are reported to be associated with AMD (Johnson and Schaefer, 2006). A systematic review showed some clinical evidence for omega-3 fatty acids protecting against AMD (Hodge *et al.*, 2006). Some results are positive (Clemons *et al.*, AREDS, 2006; Heuberger *et al.*, 2001; Smith *et al.*, 2000; Cho *et al.*, 2001; Seddon *et al.*, 2001; Mares-Perlman *et al.*, 1995), but randomised trials are needed.

12.5.2 Olfaction

There is similar evidence for the effect of DHA on olfaction. Changes in behavioural tests based on this sense were found to be due to altered brain structures rather than poorer olfaction (Catalan *et al.*, 2002). The olfactory bulb is very sensitive to a lack of dietary ALA, as this leads to a considerable reduction in its DHA content (Greiner *et al.*, 2001). Although olfactory dysfunction is common in old age, its basis is uncertain.

12.5.3 Taste

A lack of omega-3 fatty acids also affects taste. For example, animals lacking dietary ALA taste sweetness only in response to higher than normal sugar concentrations (Frances *et al.*, 1996). And ageing alters electrogustometry thresholds (Nakazato *et al.*, 2002). Like many sensory abilities, taste and smell become less acute with age, and are affected during neurodegenerative diseases (Lang *et al.*, 2006). Anosmia is a common feature of Parkinson's disease and Alzheimer's disease, and it is an intriguing observation that a premonitory sign of a disorder hitherto regarded as one of movement of cognition may be that of a disturbed sense of smell (Hawkes, 2006).

12.5.4 Audition

The auditory system changes with age (Howarth and Shone, 2006). Hearing is also affected by a lack of omega-3 fatty acids, especially the brain response. A lack of ALA also leads to accelerated or early ageing of the auditory nervous system in rats (Bourre *et al.*, 1999). The amount of DHA in the milk of lactating rats influences the auditory system of their offspring (Haubner *et al.*, 2002). The auditory systems of breast-fed infants or those fed formula supplemented with long chain polyunsaturated fatty acids for their initial 16 weeks of life mature more rapidly than the systems of infants fed a standard baby formula (Unay *et al.*, 2004).

12.5.5 The effect of age on sensory organs or brain structures

Fatty acids are important for the responses of sensory receptors and even more so for the brain sensory systems (Bourre *et al.* 1999). About half of the human cerebral cortex is involved in some aspect of visual processing. The cortex is dramatically affected by a lack of dietary ALA, as described above. Impaired odour identification in old age is associated with impaired global cognition and a more rapid decline in episodic memory and perceptual processing speed (Wilson *et al.*, 2006). The difficulty that the elderly have in identifying familiar odours is partly due to the pathological accumulation of neurofibrils in central olfactory regions (Wilson *et al.*, 2007). As ageing may induce deficits in hippocampus-dependent learning and memory, it is not surprising to find that taste memories are altered during ageing. However, peculiar organisation of memory systems related to taste during ageing cannot be totally explained by a general decline, or by decreased hippocampus function alone (Manrique *et al.*, 2007). The cochlear nucleus is the major site of projections from the auditory portion of the inner ear and the number of neurons in the cochlear nucleus and their output pathways can be reduced in parallel with age-related changes in the brain, and due to age-dependent plasticity of the cochlear nucleus in response to a loss of inputs from the cochlea (Frisina and Walton, 2006).

12.6 Desaturases, diet and antioxidants

12.6.1 Desaturases and the relationship between omega-3 fatty acids and antioxidants

ALA is desaturated and elongated in the liver. Although ageing is accompanied by a gradual decline in cell function, the liver appears to retain its function relatively well unless it is affected by some disease (Anantharaju *et al.*, 2002). But its activity is far from enough to provide sufficient DHA to other organs, including to the brain. Thus DHA must be supplied by the diet, and the advancing age can lead to changes in fat digestion. It is not clear whether the age-related reduction in apparent fat digestion is a general phenomenon affecting all fats (Peachey *et al.*, 1999), or if it involves particular fatty acids.

The activities of desaturases, particularly delta-6-desaturase (the first enzyme in the synthesis of long-chain, more unsaturated fatty acids (it acts on ALA and LA) are still to be evaluated, but they are very much less active immediately after birth, and essentially zero in the brains of animals. Their activities in the liver are greatly reduced with age (Hrelia *et al.*, 1989; Bourre and Piciotti, 1992). As a result, DHA comes either from the hepatic transformation of dietary ALA, or directly from the diet. But the capacities of astrocytes should not be neglected (Williard *et al.*, 2001). Little DHA is synthesised at the blood-brain barrier, but some may be produced at the choroid plexus as it has a high delta-6-desaturase activity (Bourre *et al.*, 1997a).

The rationale for expecting a benefit from dietary ALA is that it is the metabolic precursor of EPA and DHA. However, the extent of its conversion is actually controversial, even among investigators using similar tracer technologies. Emken *et al.* (1994) reported that as much as 15% of ALA is converted to EPA+DHA, while Pawlosky *et al.* (2001) found that only 0.2% was converted. The rate of conversion may also vary according sex, age and pathophysiological conditions (Williams and Burdge, 2006; Goyens *et al.*, 2006). The delta-6 desaturase activity is reduced in old rats fed a diet containing ALA, but is not in rats fed an ALA-deficient diet (Dinh *et al.*, 1993). Delta-desaturase activity does not only change with age, it is also influenced by the polyunsaturated fatty acid content of the diet and to the omega-6/omega-3 balance. R rats given an ALA-deficient diet and then refed a normal sufficient diet recovered only partially (Dinh *et al.*, 1995).

Hence, DHA is also considered to be an essential nutrient (Muskiet *et al.*, 2004). This is in agreement with the fact that omega-3 (and omega-6) fatty acids are essential for the brain, as initially shown in studies on foetal brain cells. These cells multiply, and take up and release neurotransmitters only if there is ARA or DHA in the medium, and not if the medium contains only LA or ALA (Bourre *et al.*, 1983; Tixier-Vidal *et al.*, 1986). Vegetarians need much more ALA than the general population because of their restricted dietary intake of DHA. ALA is converted to DHA relatively poorly and there is active competition for the enzyme involved with omega-6 fatty acids (Davis and Kris-Etherton, 2003). Further work is clearly needed to determine how much

ALA is converted to EPA and DHA (if any), especially in the brains of elderly humans.

12.6.2 Intakes of omega-3 fatty acids

ALA

The dietary intakes of omega-3 fatty acids by the young as well as adults of any country are poorly documented. This means that there is very little information on the intakes of elderly people. The French diet is clearly deficient in ALA (Legrand *et al.*, 2000; Weill *et al.*, 2002; Astorg *et al.*, 2004), as is that of other countries. (Voskuil *et al.*, 1996; Kris-Etherton *et al.*, 2002). Older people are believed to obtain less than adequate dietary ALA (and DHA) to the same extent as other adults. For instance, people aged over 65 in Australia obtain 0.98mg/DHA/day (Meyer *et al.*, 2003). A lack of dietary ALA probably leads to reduced DHA synthesis.

EPA and DHA

The estimated consumption of EPA and DHA in France indicates that adults consume twice the French RDA of DHA (Astorg *et al.*, 2004). But this varies considerably from one person to another. A study on a small sample in Brittany asked the participants not to eat animal fats (excluding fish and sea products) and found that they obtained less than half the French RDA (Weill *et al.*, 2002). Unfortunately, little work has been done on the DHA intakes of the elderly. The DHA intake of people aged over 70 living in Pennsylvania (USA) is insufficient, as their EPA+DHA intake is only 200 mg/day (Kris-Etherton *et al.*, 2002). The DHA intake is 106 mg/day in Australia (Meyer *et al.*, 2003).

Intake of DHA from seafood has been calculated recently in France for the whole population (Bourre and Paquotte, 2006), and then extrapolated to the elderly (Bourre and Paquotte, 2007). Generally speaking, people aged 55–65 consume more seafood products than do younger people, while elderly people consume much less. Even the intakes of Eskimos are now not very high (Dewailly *et al.*, 2001), although native foods (including fatty seafood) contribute significantly less to the diets of young adults than to those of the elderly, especially among women (Nobmann *et al.*, 2005).

12.6.3 Antioxidants

Cell death due to oxidative stress has been identified as of major importance in the onset of chronic diseases and ageing. The impact of anti-oxidant vitamins, such as alpha-tocopherol and vitamin C, on brain health has been examined. Any ALA or DHA added to the diet must be protected from oxidation in both the food itself and in the tissues into which it is incorporated. The ingestion of large amounts of fish oil modifies the fatty acid profile of the brains of animals without causing peroxidation (Chaudière *et al.*, 1987). The activities of desaturases are modified by vitamin E (Despret *et al.*, 1992).

Animal experiments have shown that only alpha-D-tocopherol is integrated into the membranes of the nervous system, while others, like gamma tocopherol, are not (Clement *et al.*, 1995; Clement and Bourre, 1997). It is not yet known if the ageing metabolic system discriminates between natural vitamin E and the synthetic vitamin, as does that of infants (Stone *et al.*, 2003). In humans, during ageing, there is an inverse relationship between the total concentration of tocopherols (and retinol, total carotenoids) in the whole brain and in the frontal region, but not in the occipital regions (Craft *et al.*, 2004).

Plants metabolites, like polyphenols, also seem to act as neuroprotectants, but further study on them is needed (Schaffer *et al.*, 2006).

12.7 Omega-6 fatty acids

A specific lack of linoleic acid (LA) does not appear to occur in man. It is difficult not to absorb linoleic acid, as this fatty acid is present to some extent in the majority of foods, although exceptional cases may occur in people on an artificial diet for several months. Selective, serious linoleic acid deficiency has therefore never been observed in man, perhaps because sufficiently detailed investigations have not been conducted.

Most studies deal indirectly with omega-6 fatty acids as they focus on omega-3 fatty acids and study their relationship with omega-6 fatty acids. Only the minimum dietary requirements of omega-6 fatty acids have been determined in animals (Bourre *et al.*, 1990b). The effect of an increase in dietary linoleic acid on the tissue concentration of DHA acid and consequently on ALA requirement have been documented (Bourre *et al.*, 1996). As people grow older, their diets contain less and less ARA, and this seems to be related to changes in glutamate receptors (Ulmann *et al.*, 2001).

Recovery from an omega-3 fatty acid deficiency is only possible if the dietary omega-6 fatty acids do not provide excessive competition (Ikemoto *et al.*, 2001). Omega-6 and omega-3 fatty acids modulate neurotransmitter metabolism, and they influence receptor density in the hippocampus of rats. This could account for the effects of these fatty acids on memory (Farkas *et al.*, 2002). Competition between omega-3 and omega-6 fatty acids concerns elongation and desaturation reactions, rather than recycling (Contreras *et al.*, 2001). The ratio of omega-6 to omega-3 essential fatty acids is very important, a low ratio is most desirable as it reduces the risk of succumbing to many of the chronic diseases that are prevalent in both Western societies and developing countries (Simopoulos, 2002). The consumption of foods with a well defined omega-3/omega-6 ratio can help protect against various components of stress (Yehuda *et al.*, 2002).

12.8 Omega-9 fatty acids

The main omega-9 fatty acid in the brain is oleic acid (18:1ω9), but there are also large quantities of long-chain derivatives, mainly 24:1, especially in the

myelin sheath. The nutritional value of oleic acid in a balanced diet has been the subject of a number of studies, with particular emphasis on the cardiovascular system. But this fatty acid is also important for the brain (Bourre and Dumont, 2003). Feeding rats a diet lacking oleic acid leads to a reduction of the oleic acid concentration in many organs, including the sciatic nerve, but not in the brain. Therefore, the endogenous synthesis in many organs does not compensate for the absence of oleic acid from the food (Bourre *et al.*, 1997b). This fatty acid is therefore partially essential.

There may be several explanations for why the oleic acid concentration in cerebral structures is not altered according to the oleic acid content of the diet. The nervous system may selectively bind oleic acid, perhaps by specific, active transport mechanisms across the blood brain barrier. Or it may be able to synthesise all of the oleic acid that it needs, regardless of the dietary intake, as the brain contains an active stearyl desaturase (Carreau *et al.*, 1979). The concentration of this delta-9-desaturase in the hippocampus of mice showing signs of accelerated ageing is low, which could account for their observed behavioural disturbances (Kumar *et al.*, 1999).

12.9 Saturated fatty acids

The overall mechanisms by which saturated fatty acids are synthesised in the brain and in peripheral nerves have been documented for many years (Bourre *et al.*, 1976; Murad and Kishimoto, 1978; Salles *et al.*, 2002) and the details of these reactions have been investigated (Knoll *et al.*, 1999). These mechanisms are now universally accepted, except that some lignoceric acid (C24:0) can be obtained from the diet (Bourre *et al.*, 1977; Singh *et al.*, 1984), as illustrated by the reduction of lignoceric acid accumulation in the brain by the presence of mono-unsaturated fatty acids in the diet in infants suffering from adrenoleukodystrophy. Unfortunately, most of these studies have concerned myelinisation, rather than ageing. Polyunsaturated fatty acids could be re-used to synthesise all types of fatty acids, including saturated fatty acids (Menard *et al.*, 1998).

12.10 *Trans* fatty acids

Trans mono-unsaturated fatty acids are mainly found in the diet, but they can be incorporated into nervous system membranes (Cook, 1979), including those of the peripheral nervous system (Bourre *et al.*, 1982). The influence of *trans* mono-unsaturated fatty acids on brain composition and function remains unclear (Wauben *et al.*, 2001).

The *trans* polyunsaturated fatty acids derived from ALA are taken up by the brain (Grandgirard *et al.*, 1994). Animal studies indicate that they reduce the concentrations of neurotransmitters in the developing brain (Acar *et al.*, 2002). A diet low in *trans* fatty acids is associated with a low cardiovascular mortality

rate (Kromhout, 2001), and possibly with less decline in cognitive function with age (Morris *et al.*, 2005).

Some special *trans* fatty acids are intermediates in the physiological synthesis of long chain saturated fatty acids in the nervous system, and are involved in the activity of the enzyme trans-2-3-enoyl-coA reductase (Cinti *et al.*, 1992; Knoll *et al.*, 1999). Little is presently known about the role of conjugated linoleic acid (CLA), especially rumenic acid (cis-9, trans-11).

12.11 Conclusions

A well preserved biochemical and physiological function depends on the proper functioning of all cell systems, including neurons. Successful ageing is characterised by a minimal loss of physiological functions.

Ageing has been defined as a progressive accumulation of changes that are either related to, or responsible for the increased susceptibility to diseases and death that accompanies advanced age. The molecular basis is largely unknown, but several theories suggest that the age-related deterioration of physiological functions is caused by changes in cell constituents, especially membranes. And lipids are one of the major constituents that undergo changes during ageing. The greatest changes occur in the phosholipid and cholesterol contents, as well as in the fatty acid profile of each individual phospholipid. Membrane-bound enzymes, receptors and transporters are all affected by alterations in the properties of the lipid bilayer. As phospholipids and sphingolipids (especially in myelin) are an integral part of membranes, they are undoubtedly important for the regulation of cell membrane function. Consequently, any modification of their metabolism (or of the metabolism of their fatty acids) may influence cell function, and hence, brain function.

The only foods that provide large amounts of DHA are seafood (fish and shellfish) and multi-enriched eggs (Bourre and Galéa, 2006). Some enriched meat from animals fed linseed may also be interesting sources of DHA (Bourre, 2005). The seafoods that contain most DHA are sardines, mackerel, salmon, sprats, herring, anchovies and squid, but all seafood contains appreciable quantities of DHA. Although shellfish contain little fat, they do contain appreciable amounts of DHA (Bourre and Paquotte, 2006, 2007).

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12.13 References

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13

Nutrition and bone health in the elderly

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Abstract: Osteoporosis is the main threat against bone health in the elderly population leading to fragility fractures of the hip, wrist and vertebrae. Although genetic factors play a major role for peak bone mass, which is determined before the age of 30 years, bone mineral density and bone strength may be influenced later in life. For example, sun exposure provides vitamin D, and physical activity improves bone strength and muscle fitness. Nutrition plays an important role in maintaining bone integrity in senescence. Calcium and vitamin D are crucial nutrients for the bone and usually gain the focus for nutritional measures. Dairy products and fish are rich in calcium, e.g. a glass of milk contains ~300 mg calcium. Oily fish is also rich in vitamin D, and dairy products are often fortified with vitamin D. In the very old (>80 years old) and in institutionalized elderly people supplementation with 1200 mg calcium and 20 μg (800 IU) vitamin D daily is advocated by most regulatory bodies. Whether younger postmenopausal women with manifest or increased risk of osteoporosis should also receive calcium and vitamin D supplementation is today controversial, although such treatment is advocated by many. To prevent secondary hyperparathyroidism and bone resorption circulating vitamin D should never be less than 50 nmol/l. Low body mass index shows a strong correlation to osteoporosis and fracture risk. For the elderly a sufficient energy intake is needed to avoid weight loss and underweight, i.e. BMI <22 kg/m^2. Both low and high protein intakes are associated with osteoporosis. However, recent research advocates a somewhat higher protein intake, e.g. meat and fish, for the elderly than is usually recommended, i.e. 1–1.5 g/kg body weight per day. For the elderly subjects who have sustained a hip fracture and are thin, supplementation with energy and protein is recommended. Fruit and vegetables contain anti-oxidants and phytoestrogenes, both with potentially beneficial effects on bone health. Although no human intervention studies on fruit and vegetable intake for bone health have been performed, it is safe to follow the general recommendation of five servings or 500 g fruit and vegetables/day. Oily fish

contains n-3 fatty acids, which are shown experimentally to have positive effects on bone integrity. As with fruit and vegetables, oily fish is most likely a good component of a healthy diet for the elderly, i.e. 2–3 fish meals per week is recommended.

In conclusion, daily intake of dairy products (Calcium+vitamin D), fruit and vegetables (anti-oxidants and phytoestrogenes) combined with fish meals (Calcium+vitamin D+protein+n-3 fatty acids) several times/week in combination with daily outdoor activities providing sun exposure (vitamin D) and physical training (bone and muscle strength) will most likely reduce the fragility fracture risk in the elderly.

Key words: osteoporosis, calcium, vitamin D, protein, malnutrition, anti-oxidants, omega-3 fatty acids, caffeine, homocysteine.

13.1 Introduction

Bone health in later life is highly dependent on factors contributing to the peak bone mass achieved during adolescence, prompting the statement 'senile osteoporosis is a pediatric disease' (Dent 1973). With this in mind, the following chapter will focus on the role of nutrition in the elderly population for the integrity of bone. First the epidemiology of osteoporosis and the nutritional determinants of bone health will be discussed. Then, the current knowledge will be outlined about what specific nutrients like calcium, vitamin D, protein and energy may add to combat the inevitable bone involution during ageing, especially at high ages. Some further nutrients like antioxidants and omega-3 fatty acids with potential effects for the prevention or treatment of osteoporosis will also be reviewed. Many patients with fragility fractures, especially hip fractures, are malnourished at the time of fracture, and will emerge from the peri-operative and rehabilitation period with an even worse nutritional status. The potential effects of nutritional supplementation during the post-fracture period will also be discussed.

13.2 Epidemiology of osteoporosis

Skeletal integrity is built during adolescence, and is gradually broken down from early middle-age with an average loss of ~1% of the skeletal bone per year. Thus, osteoporosis and its sequelae, i.e. fragility fractures of the hip, vertebra and wrist, are disorders confined to the elderly part of the population. The remaining life time risk of a 50-year-old woman to sustain a fragility fracture is 50%, with about one in five being struck by a hip fracture (Van Staa *et al.* 2001). Life expectancy in affluent societies has increased from around 50 to 80 years during the last century. As indicated by the fact that 90% of all hip fractures occur in people older than 70 years (Birge *et al.* 1994) there is a close link between age and rate of hip fractures. In 2004 461 million people were aged >65 years worldwide (Kinsella and Phillips 2005). This part of the population

increases faster (1.9% annually) than any other age group (1.2%) (UN 2001). From this it is easy to deduct that fragility fractures will soon or have already reached epidemic levels. For example, the annual rate of hip fractures is estimated to increase worldwide from 1.7 million in 1990 to 6.3 million fractures in 2050 (Prentice 2004).

Hip fractures entail heavy economic burdens, i.e. direct medical costs for fracture care alone represent a greater burden than costs for stroke, breast cancer, diabetes or chronic lung disease (Miller 1999). The individual and societal burdens of osteoporosis-related illness will increase substantially through the demographic changes. The only plausible approach to meet this challenge is to identify the modifiable factors and focus on measures of primary, secondary and tertiary prevention. They all have a bearing on the elderly part of the population, although primary prevention first of all aims at maximizing peak bone mass during adolescence and to reduce bone loss during middle ages and in early menopause.

13.3 Reduced bone health: definition of osteoporosis

Throughout life there is a shifting balance between osteoblast production of new bone matrix, its mineralization and osteoclast bone resorption. Between 5 and 10% of the skeleton is exchanged annually. The skeleton comprises trabecular (20%) and cortical (80%) bone. The quality or strength of the bone is determined by its mineralization and by its macro- as well as micro-architecture. Bone mineral density (BMD) is the hallmark for the assessment of bone quality. BMD is suggested to account for ~70% of the bone strength (Faulkner 2000).

Dual energy X-ray absorptiometry (DXA) is the dominating technique to measure and monitor BMD. The spine and hip are the preferred sites for measurements. Single X-ray absorptiometry (SXA) of the wrist and Quantitative Ultra Sound (QUS) are alternative techniques.

The severity of bone loss is categorized in relation to the mean peak BMD in the healthy young individual. The World Health Organisation (1994) defines osteoporosis as a BMD of >2.5 standard deviations (SD) below the mean BMD of healthy young subjects in the same population, i.e. a T-score < -2.5 SDs. Osteopenia is a corresponding T-score of -1 SD to -2.5 SD, whereas normal BMD is a T-score of ± 1 SD (WHO 1994).

The reliability of biochemical markers of osteoblast (e.g., osteocalcin) as well as of osteoclast (e.g., C-terminal cross-linking telopeptide of type I collagen CTX) activity improves continuously as diagnostic tools, but they are still seldom used in clinical practice. There are also several clinical signs implying the presence of osteoporosis in the elderly subject, e.g. a more than 5 cm loss of height, weight below 50 kg, thoracic and neck kyfosis and tooth loss (Wilkins and Birge 2005). In the near future we will use approaches combining BMD, biochemical and clinical signs to predict fracture risk (Kanis *et al.* 2005).

The Scandinavian countries, North America and Asia have the highest rates of osteoporosis and hip fractures. Age-adjusted hip fracture rate is seven-fold lower in southern Europe than in, for example, Sweden. The reasons for this are still not clarified.

13.4 Determinants of bone health

There is a large range of factors of genetic and environmental origin that contribute to the development of healthy bone and conversely to osteoporosis. Among non-modifiable factors increasing the risk of osteoporotic fractures are female sex (oestrogen deficiency after menopause), ethnicity (being of Caucasian or Asian origin), tallness, lactose intolerance and a family history of osteoporotic fractures. Up to 60–70% of peak bone mass and skeletal integrity is genetically determined (Prentice 2001, Naganathan *et al.* 2002). How the genetic influence on bone mass is mediated is still unknown. Polymorphisms in the genes encoding for the vitamin D-receptor and oestrogen receptors have been proposed as possible mechanisms (Raisz 2005, Uitterlinden *et al.* 2006).

However, many factors regulating bone health are of modifiable origin even up to high ages. By the choice of food intake the ingested amounts of calcium, vitamin D, protein and energy can be regulated. Thus, body weight is partly voluntarily controlled. Examples of modifiable non-nutritional lifestyle factors of importance for bone health are sun exposure, physical activity and non-smoking status.

13.5 The role of calcium and vitamin D in osteoporosis

Calcium and vitamin D are critical nutrients for bone health and remain crucial targets for preventive and treatment measures of osteoporosis.

13.5.1 Calcium and bone health

More than 99% of the total body calcium content of (1000 to 1500 g) is found in the skeleton, including the teeth. The daily exchange of calcium due to bone remodelling amounts to about 700 mg. Calcium losses via faeces, urine and skin must be replaced from the food. Milk and milk products are the richest Ca-sources. It is estimated that about 80% of the calcium supply via food is provided by dairy products (Miller *et al.* 2001). Calcium is also fairly abundant in fish especially when the bones are included, e.g. sardines. Some green leafy vegetables, like broccoli and kale, provide calcium, although they can hardly substitute dairy products. A concern is that the bioavailability of the calcium in vegetables varies as phytates and oxalates in, for example, spinach and rhubarb form insoluble calcium complexes in the gut (Miller *et al.* 2001, Weaver *et al.* 1987).

The intestinal absorption of calcium depends largely on the vitamin D status of the body. The intestinal calcium absorption decreases with age. Variations in calcium intake in early life have been suggested to account for 5–10% of the variation in peak bone mass (Matkovic *et al.* 1979).

The daily calcium need is controversial as there are no clear cut associations between calcium intake and BMD and fracture risk. Intriguing is the fact that, for example, Scandinavian populations with high mean calcium intakes, i.e. >1000 mg/day, have a much higher age-adjusted fracture incidence than African populations with low intakes, i.e. <500 mg/day. Calcium retention increases with low intake, and conversely, a high intake results in an increased urinary excretion as shown in several calcium balance studies (Hegstedt *et al.* 1952, Malm 1958). The threshold level for calcium balance has been suggested to be at an intake somewhere between 500 and 1000 mg/day (Prentice 2004). There is no clear evidence that an intake above this threshold level decreases fracture risk. In Western populations it appears that calcium intakes below 500 mg/day will induce secondary hyperparathyroidism with increased PTH-levels and increased bone resorption as consequences.

The recommended daily intake of calcium varies between countries, but is usually in the range of 800 to 1200 mg per day. The group that most likely benefits from calcium supplementation is the late postmenopausal (old) women, as bone loss due to loss of oestrogen in early menopause is difficult to affect with calcium supplementation (Reid *et al.* 1995).

13.5.2 Vitamin D and bone health

Calcitriol, i.e. 1, 25 $(OH)_2$ vitamin D3 is the active metabolite of vitamin D. Its precursor cholecalciferol is provided by the skin after sunlight exposure (ultra violet radiation) or from the diet via the gut. Cholecalciferol undergoes two hydroxylation steps, the first in the liver to 25-OH-vitamin D3 (i.e. calcidiol) and further to 1, 25-$(OH)_2$ vitamin D3 (calcitriol) in the kidney. Serum level of 25-OH-vitamin D is a reliable marker of vitamin D status. Oily fish, e.g. salmon, liver and vitamin D enriched dairy products, are the best dietary sources of vitamin D.

Vitamin D plays many roles in bone health. Its main function is to promote intestinal absorption of calcium, thus it is essential for bone mineralization. Vitamin D interacts with parathyroid hormone to maintain serum calcium homeostasis by stimulating bone resorption and calcium release. When circulating levels of vitamin D underpass 30 nmol/l secondary hyperparathyroidism and subsequent bone resorption is provoked. As vitamin D receptors are abundant in many body organs and tissues, vitamin D is suggested to have many functions besides calcium regulation, of which many remain to be elucidated (Holick 2007). Of particular interest for the elderly is the increased risk of falls with low vitamin D status and the decreased risk of falls after vitamin D treatment (Bischoff-Ferrari *et al.* 2004, Boonen *et al.* 2006b, Jackson *et al.* 2007). It is suggested that vitamin D has important roles in muscular function (Mowe *et al.*

1999, Jackson *et al.* 2007), although the mechanisms for such actions are not defined yet (Shinchuk and Holick, 2007).

Vitamin D status declines with increasing age due to several factors. Dietary intake of vitamin D rich foods, e.g. fish, is usually reduced with age, which in combination with lowered gut absorption of vitamin D constitutes nutritional reasons for vitamin D deficiency. The negative effects on vitamin D production by less outdoor activity and reduced sun exposure is aggravated by a concomitant decline in skin capacity to synthesize vitamin D. Moreover, hydroxylation capacity in the kidney is decreased.

Depending on the threshold value for circulating vitamin D, 30–80% of elderly subjects may be vitamin D deficient (Melin *et al.* 1999, Bruyere *et al.* 2007, Lips *et al.* 2006). In the Euronut Seneca Study, including 11 European countries, one third of the men and half of the women had serum 25-OH vitamin D concentrations below 30 nmol/l during winter time (Van der Wielen *et al.* 1995). A multinational study on 2600 postmenopausal osteoporotic women showed thad 64% had vitamin D serum concentrations below 30 nmol/l (Lips *et al.* 2006). Moreover, the nadir of serum parathyroid hormone was reached first by serum vitamin D concentrations >35 nmol/l. In old age even small changes in lifestyle, such as reduced sun exposure, especially in the Nordic countries, and reduced dietary intake may have detrimental effects for vitamin D and consequently calcium status. Recent consensus documents and recommendations advocate serum vitamin D concentrations to exceed 50 nmol/l (Lips 2004, Nieves and Lindsay 2007, Rizzoli *et al.* 2007).

13.5.3 Vitamin D and calcium supplementation in the elderly

It is still a matter of debate whether calcium and vitamin D have to be given together, or if vitamin D alone is sufficient to achieve fracture prevention (Bischoff-Ferrari *et al.* 2005). A recent meta-analysis, evaluating 105 potential RCTs on calcium and vitamin D supplementation came to the conclusion that oral vitamin D appears to reduce the risk of hip fractures only when calcium supplementation is added (Boonen *et al.* 2007). The topic of the possible benefit of such combined treatment has been and is the issue of great controversy and much debate. Many large-scale studies have been performed in diverse populations with various risks of fracture.

Clear evidence on fracture preventive effects prevails from the combined supplementation to elderly ambulatory institutionalized women. In 1992 Chapuy *et al.* reported that 1200 mg calcium and 800 IU (20 μg) vitamin D per day given in a randomized protocol to 3270 women aged 84 years could reduce hip fracture occurrence during 18 months by 43% in parallel with a substantial increase in serum levels of 25-OH vitamin D (Chapuy *et al.* 1992). The hip fracture preventive effect remained in the same group of >3200 women after 3 years (Chapuy *et al.* 1994). Ten years later the same French research group presented confirmatory data from 600 ambulatory institutionalized women (mean age 85 years) (Chapuy *et al.* 2002). Until recently these and many similar

results (Boonen *et al.* 2006a, Larsen *et al.* 2004, Harwood *et al.* 2004, Lips *et al.* 1996, Dawson-Hughes *et al.* 1997) have resulted in liberal recommendations of calcium-vitamin D supplementation to elderly, women in particular.

However, recent results from several large studies have come to modify the recommendations. The RECORD Trial (Grant *et al.* 2005) from UK could not show fracture preventive effects of 1000 mg calcium + 800 IU vitamin D/day in 5300 elderly (>70 years old, mean age 78 years), community-dwelling subjects (85% were women) who had previously suffered from a low-trauma fracture. After two years of treatment compliance with study medication was only about 50%. Similar null results on combined supplementation (1000 mg calcium and 800 IU vitamin D per day) were reported from a study with >3000 non-demented community-dwelling women over the age of 70 years (mean age 77 years) living in UK with at least one risk factor for osteoporotic fracture, e.g. weight <58 kg, a previous fracture, smoker or maternal history of hip fracture, followed for a median of 25 months (Porthouse *et al.* 2005). After one year adherence to the treatment was 60%.

These results have been combined in a Cochrane analysis (Avenell *et al.* 2005). The conclusion was that supplementation of a combination of 1000 mg calcium and 400–800 IU (10–20 μg) vitamin D per day is still recommended for women either living in an institution or being older than 80 years. For others supplementation was questioned by the Cochrane meta-analysis.

After the Cochrane analysis was released, the Women's Health Initiative group has reported a primary preventive randomized study on >36,000 healthy post-menopausal women (mean age 62 years) using 1000 mg calcium and 400 IU of vitamin D/day with an average follow-up period of 7 years. By intention-to-treat analysis the 12% reduction in hip fractures did not reach statistical significance, whereas treated per protocol analysis revealed a 29% (95% confidence interval, 0.52–0.97) reduction in hip fracture rate (Jackson *et al.* 2006).

The overall impression from these trials is that proof of concept, namely that fracture prevention is accomplished in those who are able to adhere to the calcium and vitamin D prescription, has been achieved. The problem with many of the studies is that compliance has been too low to allow significant effects to emerge in intention-to-treat analyses. The question is not resolved and new information is continuously provided (Boonen *et al.* 2007, Rizzoli *et al.* 2007).

A sufficient calcium intake is undoubtedly essential for bone health. This is achieved most easily by the daily use of dairy products, e.g. a glass of milk or a yoghurt portion, equivalent to about 300 mg of calcium.

A sufficient vitamin D intake could be provided by exposure to sunlight, i.e. it is suggested that 6–8 minutes 2–3 times per week exposing face, arms and legs is sufficient (Holick 2002). Dietary intake of oily fish as well as of fortified milk or other dairy products are alternative ways of providing vitamin D (Lips 2004, 2007). In the Nordic countries during winter or in immobile elderly where sun exposure is difficult to achieve, supplementation of 10–20 μg or 400–800 IU vitamin D per day is advocated. This would equal about one glass of milk and a multivitamin supplement daily.

For people who have been prescribed bisphosphonates or other pharmaceutical agents to treat osteoporosis, supplementation of calcium and vitamin D is mandatory as all studies showing positive effects from treatment are performed with such basic supplementation, i.e. 800 IU of vitamin D and 1000 mg of calcium (Rizzoli *et al.* 2007).

13.6 Energy intake, body mass and bone health in the elderly

There are strong linkages between body measures and fracture. The Study of Osteoporotic Fractures Research Group has reported prospective epidemiological data of 7000 white women aged over 66 years. A weight loss of more than 5% during 5.5 years was followed by a 1.8 times (95% confidence interval (CI) 1.43–2.24) increased risk of hip fracture, totalling 192, during the subsequent 4.4 years (Ensrud *et al.* 2003). In parallel, a nearly doubled rate of hip bone loss was noticed in the weight-losing subjects. Except from contributing to osteoporosis, a low energy intake leads to emaciation and reduced padding effect over the trochanteric region during falls. Moreover, emaciation is associated with sarcopenia and increased inclination for falls. Protein-energy malnutrition is reported in up to 50% of patients admitted due to a hip fracture (Ponzer *et al.* 1999).

13.7 Protein and bone health in the elderly

There is controversial evidence on the relation between protein and bone health (Barzel and Massey 1998, Heaney *et al.* 1998). The fact that protein consumption is highest in countries with a high prevalence of fractures is in line with epidemiological prospective data indicating that high protein intakes, i.e. more than 1.5 g/kg of body weight and especially of animal origin (Meyer *et al.* 1997), is associated with higher rates of osteoporotic fractures (Feskanich *et al.* 1996). On the other hand, there are several epidemiological indications of positive associations between protein intake and BMD (Michaelsson *et al.* 1995, Devine *et al.* 2005).

Elderly women at the highest risk of fracture have protein intakes well below the recommended dietary allowance limit (Kerstetter *et al.* 2003a). A case–control study on 1167 hip fracture patients and 1334 age and sex-matched subjects reported that with increasing quartiles for protein intake, based on food frequency questionnaires (FFQ), the odds ratio for hip fracture decreased, from 1 (lowest quartile, reference) to 0.35 (95% CI 0.21–0.59) (highest quartile), thus indicating a 65% reduction in the risk of hip fracture with a high protein intake (Wengreen *et al.* 2004). Similar data on augmented bone loss with low protein intake was previously reported from 615 elderly participants of the Framingham cohort (Hannan *et al.* 2000). FFQ revealed a mean protein intake of 68 g/day at baseline. Four years later persons in the lowest quartile of protein intake had lost

about 4% of femoral neck and lumbar spine BMD as compared to 1% ($p < 0.01$) in the corresponding sites among subjects in the highest quartile of protein intake.

Some of the controversy about protein and bone integrity originates from the fact that high protein intakes, i.e. >~2 g protein/kg body weight, increase urinary calcium excretion (Kerstetter *et al.* 2003b, Kerstetter and Allen 1994). However, it has recently been shown that this is probably an effect of increased intestinal calcium absorption, rather than of increased bone resorption (Kerstetter *et al.* 2005). On the other hand, low protein intake, i.e. below 1 g protein/kg body weight, is detrimental for bone strength for several reasons, e.g. decreased intestinal calcium absorption and secondary hyperparathyroidism (Kerstetter *et al.* 2003a). Thus, both low and high protein consumption can be detrimental for bone health. A protein intake between 1 and 1.5 g/kg body weight appears to be safe and is probably optimal (Illich and Kerstetter 2000).

13.8 Nutritional treatment after a hip fracture

About 1% of the total population in affluent countries suffer from fragility fractures every year. A hip fracture is a devastating event. Within the first year of the hip fracture around one in four dies, which corresponds to a 10–15% higher risk of mortality in fractured subjects compared to others of the same age and sex. A great proportion of these people are not able to return to their previous living as only one quarter regain their previous level of functioning.

In the fracture aftercare not only osteoporosis, but also sarcopenia need to be targeted. Both are consequences of undernutrition and inactivity. Sarcopenia is a main obstacle for recovery, and its combat remains a key goal for rehabilitation after hip fracture. Nutritional interventions in a wide perspective play a major role (Marks *et al.* 2003). In the latest meta-analysis update from the Cochrane collaboration on nutritional supplementation for hip fracture aftercare (Avenell and Handoll 2004) a total of 17 (out of a 48 possible) studies are included, comprising 1266 patients. The overall conclusion from the Cochrane collaboration report remains that oral multinutrient feeds, e.g. protein and energy fortified liquid supplementation, may reduce the risk of unfavourable outcomes, i.e. death and complications combined, with a relative risk of 0.52 (95% CI 0.32–0.84). In the much cited study by Schurch *et al.* (1998) supplementation of 20 g protein daily up to six months after hip fracture in 82 patients increased IGF-1 and BMD significantly. Tengstrand *et al.* (2007) and Tidermark *et al.* (2004) also reported positive effects on BMD, activities of daily living (ADL) and quality of life in elderly emaciated female patients with a cervical hip fracture who received 200–400 kcal and 10–20 g protein extra up to six months after the fracture.

13.9 Other nutrients of potential importance for bone health

13.9.1 Fruit and vegetables: anti-oxidants

Free radicals like superoxide and hydrogen peroxide that are produced during oxygen metabolism have the capability of inducing osteoclast activity (Sheweita and Khoshhal 2007). In one study, higher serum levels of thiobarbituric acid reactants (TBARS), i.e. a marker for lipid peroxidation, together with decreased total antioxidant power, were reported in osteoporotic women as compared to age-matched controls (Yousefzadeh *et al.* 2006). Therefore, the integrity of the anti-oxidant system is of importance for maintaining bone health. Intake of nutrients with anti-oxidative effects is a major component of the anti-oxidative defence. Especially fruit and vegetables are rich in polyphenols, flavonoids, genistein, vitamin C and vitamin E. Some, like flavonoids, genistein, and lignans, are also phytoestrogens, i.e. plant products that act on the estrogen receptors (Setchell and Lydeking-Olsen 2003), possibly without having the estrogen side effects. One possible phytoestrogen effect is an increased production of bone morphogenetic proteins (BMP) (Mundy 2006), which is a family of growth factors involved in the differentiation of osteoblasts. Thus, fruit- and vegetable-derived anti-oxidative agents have the potential to both decrease bone resorption and to increase bone formation.

Accordingly, there are several epidemiologic data that show associations between high intakes of fruit and vegetables and greater bone mineral density (Prynne *et al.* 2006, Tucker *et al.* 1999, Chen *et al.* 2006), whereas fracture data are scant. In an experimental study, intake of onion and 14 other vegetables, common in human food, by rats for four weeks increased bone mineral content. The effect mimicked that of calcitonin (Muhlbauer and Li 1999). Human intervention studies with BMD or fracture data as end-points are sparse. Arjmandi *et al.* (2002) randomized 58 post-menopausal women to dried plums (rich in phenolic and flavonoid compounds) vs. dried apples. Small positive effects on insulin-like growth factor-I and on bone-specific alkaline phosphatase were achieved.

Although there are few strong treatment data on the effects on osteoporosis by fruit and vegetables there are reasons, mainly based on epidemiologic data, to encourage increased consumption of fruit and vegetables even for the sake of bone health. Side effects are few and mild. Most regulatory bodies worldwide recommend at least five servings of fruit and vegetables per day, which would equal about 500 grams per day.

13.9.2 Omega-3 fatty acids

Eicosanoids derived from fatty acids (FA) have important effects on bone formation. It is well established that prostaglandin (PG) E2 derived from arachidonic acid (AA, an n-6 FA) attenuates bone formation (Klein and Raisz 1970, Raisz 2005). Marine n-3 FA, e.g. eicosapentaenoic acid (EPA), competes with AA for PG production, leading to generation of PGE3 that is less potent than PGE2. Thus, increased n-3 FA intake has the potential to act beneficially on

bone metabolism (Albertazzi and Coupland 2002). FAs are also known to affect cytokine induced inflammation as intake of n-3 FA reduce the generation of interleukins and tumour necrosis factor from blood mononuclear cells. Several lines of evidence link inflammation to osteoporosis, for example via increased osteoclast activity (de Martinis *et al.* 2006), providing another mechanistic clue why n-3 FA might be beneficial.

Several experimental studies in ovariectomized animals support the assumption that n-3 FA may protect against osteoporosis. In one study provision of dietary omega-3 fatty acids reduced osteoclast activity and promoted bone growth (Sun *et al.* 2003). Another animal study showed that an EPA-enriched diet prevented bone loss caused by oestrogen deficiency and inadequate calcium nutrition, and maintained bone strength (Sakaguchi *et al.* 1994). A six-month study showed that n-3 FA rich fish oil supplementation to ageing mice was associated with higher BMD, lower osteoclast generation and higher osteocalcin levels than corn oil (n-6 FA) supplementation (Bhattacharya *et al.* 2007). N-3 FA induced decrease in cytokine activity was suggested to be of causal importance.

Epidemiologic studies on the relation between fatty acids and bone health are sparse. Cross-sectional data was reported from the Rancho Bernardo Study which show that low n-6 to n-3 ratios as indicated from food frequency questionnaires were associated with higher BMD in about 1500 community-dwelling subjects between the ages of 45 and 90 years (Weiss *et al.* 2005). In a prospective Swedish study on 78 healthy young men, serum phospholipid levels of n-3 FA at 22 years of age were positively associated with bone mineral retention between ages of 17 and 22 years (Hogström *et al.* 2007).

Only a few small intervention studies have been performed in humans, summarized in the review by Albertazzi and Coupland from 2002. In the three studies, reported between 1995 and 2000, a mixture of n-6 (linoleic and gamma linoleic acid) and n-3 (EPA/DHA) FA were used as active treatment. A four-month study in 40 osteoporotic patients indicated positive effects on serum markers of bone formation (van Papendorp *et al.* 1995). A small positive effect on BMD was shown in one study of 65 postmenopausal women given PUFA treatment for 18 months (Kruger *et al.* 1998), whereas no effect on either BMD or bone turn over markers could be observed by 12 months PUFA treatment to 42 postmenopausal women (Bassey *et al.* 2000).

Today, the evidence for health benefits by increasing the intake of fat fish and n-3 fatty acids is fairly strong when it comes to cardiovascular disease. However, before we can give any firm recommendations for increased fish/n-3 intake in order to promote bone health we need more clinical trials as well as better understanding of the physiological effects on bone metabolism by n-3 FA (Vanek and Connor 2007).

13.9.3 Caffeine

Caffeine in coffee has been claimed to increase the risk of osteoporotic fractures. Some experimental studies indicate that caffeine might impair osteoblast

activity (Tsuang *et al.* 2006) or decrease vitamin D receptor expression (Rapuri *et al.* 2007). In a large Swedish epidemiological cohort of >30,000 women (40–76 years) it was reported that the women consuming >330 mg caffeine daily, equivalent to >600 ml coffee (~4 cups)/day, had a slight increase (HR 1.33 (95% CI 1.07–1.65)) in 10-year fracture incidence. This increased risk was confined to those women with the lowest calcium intake (Hallström *et al.* 2006). Thus, provided that the calcium intake is sufficient, the evidence for detrimental effects of coffee on bone health is weak (Heaney 2002).

13.9.4 Vitamins B12, K and A

Elevated homocysteine (Hcy) serum concentrations was 2004 in two separate large observational studies reported to be associated with osteoporotic hip fractures (McLean *et al.* 2004, van Meurs *et al.* 2004). This relationship has then been verified in several epidemiological studies. Attempts have been made to find possible mechanisms. So far it is not resolved whether the bone detrimental effects are due to toxic effects from Hcy or explained by an underlying deficiency of vitamin B12, B6 or folic acid (McLean and Hannan 2007). Meat, milk, fish and liver contains vitamin B12, whereas vegetables, legumes and fruits provide folic acid. Whether increased intake of such food stuffs or the supplementation of the B vitamins in order to normalize circulating Hcy may decrease the risk of fragility fractures is still not known.

Vitamin K, abundant in green vegetables like broccoli and kale and in soy beans, has been suggested to play a positive role in bone formation (Nieves 2005). In experimental studies provision of vitamin K analogues to ovariectomized rats has protected against bone loss (Iwamoto *et al.* 2006). Epidemiological data also indicate that patients with osteoporotic fractures have low circulating vitamin K (Hodges *et al.* 1993). Clinical trials of the effects on vitamin K supplementation in order to prevent osteoporosis or fragility fractures are few and not conclusive (Booth 2007).

Vitamin A has attracted a great deal of interest as a factor involved in bone health (Ribaya-Mercado and Blumberg 2007). However, a fairly large number of observational studies have come to inconsistent results and no firm conclusions on the possible adverse (e.g., Melhus *et al.* 1998, Michaelsson *et al.* 2003) or beneficial (e.g. Barker *et al.* 2005) effects from vitamin A can be drawn.

13.10 Conclusions

Osteoporosis is the main threat to bone health in the elderly population leading to fragility fractures of the hip, wrist and vertebrae. Although genetic factors play a major role for peak bone mass, which is determined before the age of 30 years, bone mineral density and bone strength may be influenced later in life. For example, sun exposure provides vitamin D, and physical activity improves bone strength and muscle fitness. Nutrition plays an important role in

maintaining bone integrity in senescence. Calcium and vitamin D are crucial nutrients for the bone and usually gain the focus for nutritional measures. Dairy products and fish are rich in calcium, e.g. a glass of milk contains ~300 mg calcium. Oily fish is also rich in vitamin D and dairy products are often fortified with vitamin D. In the very old (>80 years old) and in institutionalized elderly people supplementation with 1200 mg calcium and 20 μg (800 IU) vitamin D daily is advocated by most regulatory bodies. Whether younger post-menopausal women with manifest or with increased risk of osteoporosis should also receive calcium and vitamin D supplementation is today controversial, although such treatment is advocated by many. To prevent secondary hyperparathyroidism and bone resorption circulating vitamin D should never be less than 50 nmol/l. Low body mass index show a strong correlation to osteoporosis and fracture risk. For the elderly a sufficient energy intake is needed to avoid weight loss and underweight, i.e. BMI <22 kg/m^2. Both low and high protein intakes are associated with osteoporosis. However, recent research advocates a somewhat higher protein intake, e.g. meat and fish, for the elderly than is usually recommended, i.e. 1–1.5 g/kg body weight per day. For the elderly subjects who have sustained a hip fracture and are thin, supplementation with energy and protein is recommended. Fruit and vegetables contain anti-oxidants and phyto-estrogenes, both with potentially beneficial effects on bone health. Although no human intervention studies on fruit and vegetables intake for bone health have been performed it is safe to follow the general recommendation of five servings or 500 g fruit and vegetables/day. Oily fish contains n-3 fatty acids, which are shown experimentally to have positive effects on bone integrity. As for fruit and vegetables, oily fish is most likely a good component of a healthy diet for the elderly, i.e. 2–3 fish meals per week is recommended.

In conclusion, daily intake of dairy products (Calcium+vitamin D), fruit and vegetables (anti-oxidants and phytoestrogenes) combined with fish meals (Calcium + vitamin D + protein + n-3 fatty acids) several times/week in combination with daily outdoor activities providing sun exposure (vitamin D) and physical training (bone and muscle strength) will most likely reduce the fragility fracture risk in the elderly.

13.11 References

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14

Nutrition and immune function in the elderly

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Abstract: Immune responses are particularly influenced by nutritional status in aged persons. In very healthy elderly, immune responses decline only in nonagenarians, but far sooner in frail and diseased elderly. Frailty, often associated with decreases in micronutrient status, is associated with decreased cell mediated immune (CMI) responses and may be reversed with micronutrient supplementation. Protein energy malnutrition (PEM) is linked to decreased CMI and leads to a vicious circle from PEM to diseases to PEM and is difficult to reverse without high energy intakes.

Key words: immune responses, nutrition status, inflammation, frailty.

14.1 Introduction

Immune responses decrease with advancing age. Owing to this fact, elderly people are prone to frequent infectious diseases, to more infection-related deaths, to increased frequency of cancer and, in general, to increased complications in most diseases (Miller, 1996). Over the past twenty years, it has been reported that the immune system ages differently in different categories of aged people and that its ageing process is highly dependent on health status (Lesourd and Mazari, 1999; Lesourd, 1999). In fact, in the 'ageing-well' population, decline of the immune system is observed only in very elderly people (> 90 years of age), while it appears at a younger age in the frail elderly (Lesourd and Mazari, 1999; Lesourd, 1999; Ahluwalia, 2004). This points to the interaction of the immune system with environmental factors in immune ageing,

including diet and nutritional status. In view of this, three different types of immune ageing should be considered:

1. healthy ageing, characterized by a late decline in immune responses, mainly in cell-mediated immunity (CMI);
2. common ageing, observed in most individuals, characterized by an earlier decline in CMI and by lower antibody responses in relation to lower micronutrient status;
3. pathologic ageing, mostly related to decreased protein-energy status, probably linked with ongoing subclinical inflammatory processes.

This article briefly reviews the different forms of immune ageing and the influence of nutritional factors.

14.2 Immune responses in the very healthy elderly: primary immune ageing

Immune responses include responses to specific antigens either by cells (T-cells responsible for cell-mediated immunity) or through antibody production (B-cells responsible for humoral immunity), as well as non-specific immune responses (functions of monocyte-macrophages and/or polymorphonuclears). Figure 14.1 represents the different interactions between immune cells after antigen stimulation.

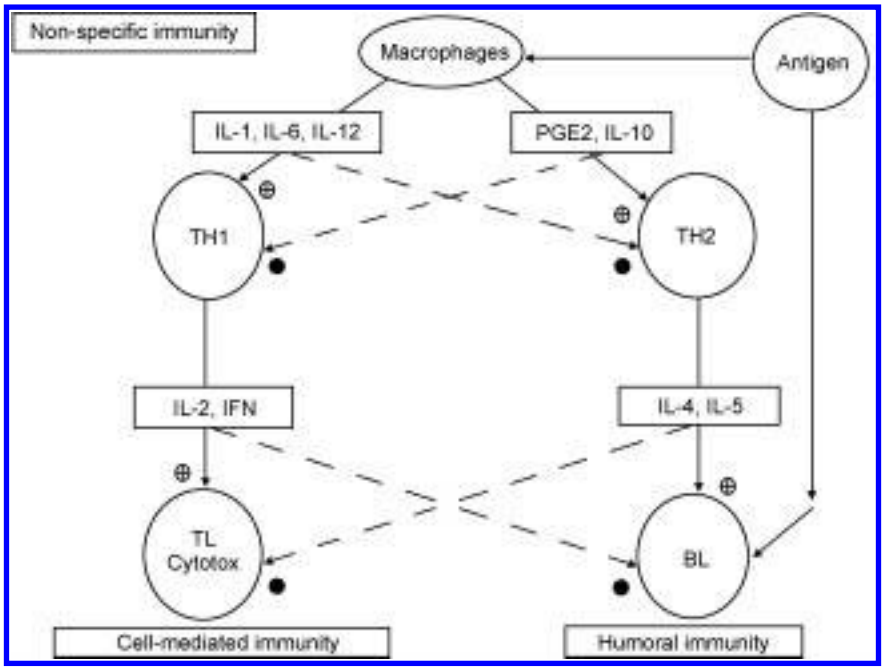

Fig. 14.1 Different interactions between immune cells after antigen stimulation.

Immune ageing was first studied (in the 1980s) using the SENIEUR protocol defined for *a priori* characterized healthy elderly (Ligthardt *et al.*, 1984). Nevertheless, it rapidly became obvious (early 1990s) that the criteria for healthiness included in the SENIEUR protocol were insufficient, since discrepancies were reported in different publications. Therefore new criteria were used to check healthiness, including, amongst others, the absence of chronic diseases and of drug use, and the presence of 'normal' macronutrient and later micronutrient status (Lesourd and Mazari, 1999; Wick and Grubek-Loebenstein, 1997). Using these criteria, it rapidly became clear that age-related changes are reported in immune responses, but that they occur far later in life than previously reported, mainly in nonagenarians (Ahluwalia, 2004).

Immune ageing is mostly reported as a decline in CMI responses, while antibody responses and non-specific immunity seem relatively preserved until very old age (Lesourd and Mazari, 1999; Ahluwalia, 2004; Mazari and Lesourd, 1998; Ahluwalia *et al.*, 2001).

14.2.1 T-cell subsets

T-cell subsets change in late life with a low decline in the 'mature' CD3+ subset (Lesourd and Mazari, 1999; Mazari and Lesourd, 1998; Ales-Martinez *et al.*, 1988; Lesourd and Meaume, 1994; Lesourd *et al.*, 1994), though this is not always observed (Pawelec *et al.*, 2001), or is partly compensated by an increase in the CD2+CD3- subset (Lesourd and Mazari, 1999; Mazari and Lesourd, 1998; Ales-Martinez *et al.*, 1988; Lesourd and Meaume, 1994; Lesourd *et al.*, 1994) (Table 14.1). T-cells first mature in the liver during early pregnancy and later, in late pregnancy and during life, in the bone marrow. The decline in the CD3+ subset might, therefore, be related to an earlier decline in thymus function, since CD2 and CD3 are acquired during thymus maturation of T-cells, CD2 being the first CD to appear on cell membrane and CD3 the latest.

Therefore the occurrence of CD2+CD3- subset may be due to incomplete thymus maturation of T lymphocytes, the latest CD3+ occurs later on the lymphocyte membrane. However, it has been suggested that in very aged mice (Barrat *et al.*, 1999) and in men (Lesourd and Mazari, 1999), T-cell maturation also occurs partly in the liver, which may be either a compensative phenomenon for decreased thymus functions and/or the indication of an ongoing phenomenon not observed at adult age when the thymus is very active (Lesourd and Meaume, 1994). Whatever the maturation site, the decrease of the blood CD3+ subset leads to decreases in lymphocyte proliferation since the CD3- subset has a lower ability to proliferate than the CD3+ subset (Ales-Martinez *et al.*, 1988).

During life, other T-cell subsets also change. From birth to early adulthood, naïve T-cells, quantified by CD45RA+, decrease and are progressively replaced by memory CD45R0+ T-cells (Cossarizza *et al.*, 1992), in relation to antigen boost. This switch mostly occurs until the age of 30, and it continues thereafter, but at a far lower speed (Cossarizza *et al.*, 1992). This switch from CD45RA+ to CD45R0+ also induces a decline in the ability of peripheral lymphocytes to

Table 14.1 Subsets and functions of peripheral blood T lymphocytes from subjects of different ages. Subjects were recruited using the SENIEUR protocol and added criteria (Lesourd and Mazari, 1999)

	Very healthy young adults n = 65	Very healthy young elderly n = 69	Very healthy self-sufficient old elderly n = 35
Age (years)	30.1 ± 5.7	79.1 ± 6.3	93.6 ± 4.1
Albumin ($g\,l^{-1}$)	43.4 ± 4.2	42.8 ± 3.7	41.6 ± 3.8
CD3+ cells (number μl^{-1})	1885 ± 543	1672 ± 476	1354 ± 321‡*
CD2+CD3- (number μl^{-1})	115 ± 136	136 ± 158	259 ± 187‡**
IL- 2 production ($ng\,l^{-1}$)$^{\$}$	2.05 ± 0.32	1.84 ± 0.39	1.28 ± 0.37†**
IL-6 production ($ng\,l^{-1}$)$^{\$}$	1.42 ± 0.41	1.73 ± 0.51*	1.97 ± 0.46*
Lymphocyte proliferation$^{£}$ (10^3cpm 10^6 $cells^{-1}$)	153 ± 41	129 ± 35	78 ± 37‡***

IL, interleukin
Significant differences from very healthy young adults * $p < 0.05$, ** $p < 0.01$, ***$p < 0.001$
Significant differences from very healthy young elderly † $p < 0.05$, ‡ $p < 0.01$
$^{\$}$ determined using 5 μg mitogen 10^6 $cells^{-1}$
$^{£}$ determined using 1 μg mitogen 10^6 $cells^{-1}$

proliferate, since CD45R0+ cells have a lower ability to divide rapidly than CD45RA+ cells (Hobbs and Ernst, 1997). After the age of 50, and even far later in the very healthy elderly, T-Helper cells of type 1 (TH1), quantified by decreases in interleukin 2 (IL-2) secretions decline, with the result that later on T-Helper cells of type 2 (TH2), quantified by interleukin 4 (IL-4) releases, overcome TH1 (Cakman *et al.*, 1996; Shearer, 1997). This TH1/TH2 disequilibrium may explain the age-related decreases in CD8+ cytotoxic T-cells observed in aged persons (Mazari and Lesourd, 1998; Lesourd and Meaume, 1994; Lesourd *et al.*, 1994). This irreversible CD switch leads to a higher incidence of infectious diseases, as was observed in the case of HIV (Clerici and Shearer, 1994). In fact, a switch of this kind accelerates the decline in CMI functions (Lesourd, 2004). Both switches, CD45RA+ to CD45R0 and TH1 to TH2, are due to antigenic pressures throughout life and occur sooner when infection rates are higher (Lesourd, 2004). Therefore two different factors cause the T-cell subsets to age: a decline in thymus functions and antigenic pressures.

Nevertheless, these changes are only observed at very old age in carefully selected elderly (Lesourd and Mazari, 1999; Ahluwalia, 2004; Wick and Grubek-Loebenstein, 1997; Mazari and Lesourd, 1998; Ahluwalia *et al.*, 2001). For example, decreased IL-2 secretion, as a function of the TH1 subpopulation, is only observed in nonagenarians (Lesourd and Mazari, 1999; Mazari and Lesourd, 1998). Nevertheless, at that age a decrease in the CD8+ subset, which follows a decrease in the TH1 subpopulation, is not observed in carefully selected elderly people with all criteria of healthiness (Wick and Grubek-Loebenstein, 1997). This indicates that some of the effects of immune ageing are not observed even in the very old when they are still healthy.

14.2.2 T-cell functions

T-cell functions are generally reported to decline with ageing, since interleukin 2 (IL-2) release and lymphocyte proliferation from mononuclear cell cultures have been shown to decrease in the elderly (Ales-Martinez *et al.*, 1988; Lesourd and Meaume, 1994; Rabinowich *et al.*, 1985; Nagel *et al.*, 1988; Murasko *et al.*, 1987; Pawelec, 2003) (Table 14.1). Such changes have been reported to be linked to the T-cell subset changes (Lesourd and Mazari, 1999; Ahluwalia, 2004; Mazari and Lesourd, 1998; Ahluwalia *et al.*, 2001; Ales-Martinez *et al.*, 1988), but also to changes in membrane viscosity related to changes in lipid composition (Fulop *et al.*, 2005), and in particular to a decrease in CD28+ cells (Boucher *et al.*, 1998). The CD28 molecule is of great importance for T-cell activation in cooperation with the macrophages (Nel, 2002). In fact, in carefully selected individuals, changes are observed only in the very old (> 90 years) but not in the younger elderly (70–85 years) (Lesourd and Mazari, 1999; Ahluwalia, 2004; Wick and Grubek-Loebenstein, 1997; Mazari and Lesourd, 1998; Ahluwalia *et al.*, 2001; Wick *et al.*, 1991). Similar findings were observed for the ability to release IFNγ (Sinderman *et al.*, 1993) or IL-12 (Mbawuike *et al.*, 1997), other cytokines released by the TH1 subset. It has even been reported that nonagenarians have comparable responses to young adults (Proust *et al.*, 1982). In fact, in the very old population, higher frequencies of phenotypes associated with higher CMI responses are found (Proust *et al.*, 1982). Therefore it is widely speculated that some phenotypes associated with high immune responses may be an advantage in order to live longer. This has been observed in mouse strains (Kubo and Cinader, 1990). In summary, T-cell functions do decline with ageing, but only at a very old age in the very healthy elderly.

14.2.3 B-Cells: humoral immunity

Age-related changes in humoral immune responses (functions of B lymphocytes) are altogether more subtle. Immune responses to foreign antigens decline, while responses to self antigen increase (Lesourd, 2004). Changes in B-cell subsets (Weksler, 1995) seem to be associated with the observed modifications of antibody production, which are also partly due to changes in TH1/TH2 equilibrium (Castle *et al.*, 1997; Mysliwska *et al.*, 1998). Indeed, CD5– B-cells, which produce antigen-specific antibodies, decrease and are partly replaced by CD5+ B-cells, which are responsible for the production of regulatory antibodies, i.e. anti-idiotype-auto-antibodies (Weksler, 1995). The increase in regulatory anti-idiotypes is responsible for the decrease in antigen-specific antibody, as shown in mice (Goidl *et al.*, 1983) and humans (Arreaza *et al.*, 1993). This may be due to the increasing TH2/TH1 ratio during late life (Castle *et al.*, 1997; Mysliwska *et al.*, 1998), which induces relative increases in antibody production. This occurs in all antibodies, firstly in antigen-specific antibodies and consequently in regulatory anti-idiotype antibodies which block the production of the antigen-specific antibodies. The result is that repeated antigen stimulations throughout life progressively lead to fewer and fewer antigen-

specific antibodies, and to more and more non-specific antibodies which include regulatory anti-idiotype antibodies (Arreaza *et al.*, 1993; Muller *et al.*, 1986). These changes of B-cell subsets are probably only the reflection of such changes due to antigen pressure throughout life.

In addition to the observed changes in antibody quality and/or specificity, antibody production also declines with age (Goidl *et al.*, 1983; Muller *et al.*, 1986). These changes are probably of little clinical significance since antibody responses after vaccination are comparable between the healthy elderly and their younger counterparts (Moulias *et al.*, 1995; Huang *et al.*, 2002).

14.2.4 Non-specific immunity

Non-specific immunity (involving polymorphonuclear and macrophage functions) appears to be relatively preserved, and even enhanced, with ageing. Macrophage proinflammatory cytokines are sustained (Nafziger *et al.*, 1993) or even enhanced (Lesourd, 2004; Ershler *et al.*, 1993) in very old adults, even when they are apparently healthy (Lesourd, 2004). This may be a compensatory phenomenon to decrease T-cell activation by macrophages (macrophages present the antigen to T-cells) in relation to decreased CD28 expression by T-Cells (Nel, 2002). This may also be a sign of the permanent activation of macrophages. Indeed, macrophages permanently release more prostaglandin E2 and more free radicals (Hayek *et al.*, 1997), an important phenomenon of the ageing process (Das *et al.*, 2007). In addition, stress responses induced by the macrophages are long-lasting in aged rats (Sapolski *et al.*, 1983) and recovery lasts longer in the elderly (Weng, 2006). Such higher and/or longer macrophage responses may be the consequence of decreased T-cell functions, which are boosted by the prolonged macrophage activation. Indeed, the T-cells of aged persons are more responsive to a suppressive effect of PGE2 than those of younger counterparts (Goodwin, 1992). Furthermore, when the elderly are treated with the radical scavenger vitamin E, macrophage Ros Oxygen Species (ROS) decrease and T-cell response increases (Meydani *et al.*, 1990). Therefore, the permanent activation of macrophages may be an important component of, and may even lead to, the dysregulation of the immune responses observed in elderly people (Meydani *et al.*, 1990). In other words, decreased T-cell functions are responsible for increased macrophage activation in order to induce sufficient T-cell responses to face antigen aggression. This increase in macrophage activation induces a further decrease in T-cell functions, causing the macrophages to be even more active. The observed permanent low levels of the inflammatory process are only the reflection of this dysregulation (Chung *et al.*, 2006). As a consequence, T-cell functions are reduced and this leads to a delay in recovery time (Weng, 2006).

14.2.5 Overview

T-cell functions slowly decline during the ageing process, but this effect is only seen at very old age in the very healthy elderly. This decline is the result of two ageing phenomena: a decrease in thymus functions that starts early in life at

puberty, and antigenic pressure throughout life that leads to the production of more dividing T-cells, which become less and less efficient due to the production of less mature T-cells. Decreased T-cell functions may induce a compensative increase in macrophage functions which, on the other hand, induce a further decrease in T-cell functions. Ageing, therefore, appears to induce dysregulation of the immune system that progressively reduces its ability to react appropriately to antigenic stimulations, leading to lower and/or less adapted responses. Environmental factors, such as antigenic pressure and inadequate nutrition, accelerate the ageing process.

14.3 Immune responses in the frail elderly: common or secondary immune ageing

Immune responses are influenced by environmental factors (Lesourd *et al.*, 1998). Indeed, CMI responses are decreased in healthy persons with micronutrient deficits (Lesourd *et al.*, 1998). This has been shown for numerous micronutrients acting on CMI in the elderly, such as vitamin B_6 (Talbott et al., 1987; Rall and Meydani, 1993), B_9 (Lesourd, 2004; Lesourd *et al.*, 2002), zinc (Keen and Gershwin, 1990; Prasad *et al.*, 1993) and antioxidants (Meydani *et al.*, 1995; Hughes, 2002). Nutritional deficiencies have a great influence on immune responses in the frail elderly, whose macrophages exhibit decreased pro-inflammatory functions (Uyemura *et al.*, 2002). In addition, anti-inflammatory responses are increased in these frail elderly, which may explain the decreased CMI responses (Uyemura *et al.*, 2002). These CMI responses, such as lymphocyte proliferation and IL-2 release, have also been shown to be decreased in self-sufficient, home-living but apparently healthy elderly (Lesourd and Mazari, 1999; Ahluwalia, 2004; Lesourd, 2004; 2006). The decreased CMI responses in these healthy elderly are probably due to micronutrient deficits. The latter influence is of great importance in common ageing since one-third to half of the 75-year-old, self-sufficient, home-living elderly exhibited insufficient nutritional intake for at least one micronutrient acting on the immune system (Lesourd, 2006). Indeed, decreased CMI responses were first observed in the apparently healthy elderly (Lesourd and Meaume, 1994; Lesourd *et al.*, 1994), but after careful selection of healthy persons with micronutrient deficits (Lesourd and Mazari, 1999; Mazari and Lesourd, 1998), these changes were not observed. It has been claimed that nutritional status predicts T-cell subclass levels and T-cell function in apparently healthy elderly people (Molls *et al.*, 2005).

14.3.1 Single nutrient supplementation

Scientific evidence of the role of micronutrient deficits in decreased CMI responses in the apparently healthy elderly comes from supplementation studies. Numerous controlled supplementation studies have shown that the restoration of

deficient micronutrient status enhances immune responses in apparently healthy or frail elderly people (Lesourd and Mazari, 1999; Ahluwalia, 2004). The first study, published in 1987, showed that a physiologic dose (500 mg/d) of pyridoxine induces increases in lymphocyte proliferation after two months of supplementation (Talbott *et al.*, 1987). This effect was only obtained in subjects with initially low blood levels of pyridoxine, showing that the effect was due to restoration to 'normal' blood levels for this vitamin. Since then, similar studies have appeared for other micronutrients, providing zinc supplements to zinc-deficient individuals (Prasad *et al.*, 1993; Boubaika *et al.*, 1993; Prasad, 2000), or folic acid to subjects with normal levels but with values in the lowest part of the normal range (Lesourd, 2004). These promising studies also point out possible additional effects of such supplements. Prasad (2000) has shown that zinc supplementation not only improves zinc status, but it also decreases copper status, another nutrient acting on the immune system. Furthermore, it has also been shown that high dose zinc supplementation ($\leq$100 mg/d) is detrimental to immune responses (Chandra, 1984; Bogden *et al.*, 1994; reviewed in Dardenne, 2006).

From these studies, it is obvious that restoration of nutritional deficits with the appropriate micronutrient may be helpful in restoring immune responses, but that such supplements must be given cautiously. Furthermore, micronutrient supplements are not only useful in the case of micronutrient deficits, but also when micronutrient status is either in the lower range of normality, as shown for folic acid (Lesourd, 2004), or sometimes even in the absence of micronutrient deficiency, as shown for vitamin E (Meydani *et al.*, 1990; 1995; 1997; Park *et al.*, 2003). Nevertheless, if supplementation is performed, the supplements must be given with caution since a recent meta-analysis has shown that antioxidant supplementations may be dangerous (Bjelakovic *et al.*, 2007), particularly in diseased persons (Graat *et al.*, 2002).

14.3.2 Multi-nutrient supplementation

Similar effects have been observed using multi-supplements, including either combinations of antioxidant micronutrients (Penn *et al.*, 1991; Galan *et al.*, 1997; Girodon *et al.*, 1997; 1999) or combinations of multi-trace-elements and vitamins (Bogden *et al.*, 1990; 1994; Chandra, 1993; Pike and Chandra, 1995; reviewed in Lesourd and Mazari, 1999). Some of these studies have even shown that multi-supplements may have clinical effects, and that they not only restore immune responses, but also reduce the rate and duration of infections in home-living (Chandra, 1993) or in institutionalized (Girodon *et al.*, 1997) frail elderly, when given on a long-term basis ($\geq$ one year). Nevertheless, these results needs to be examined cautiously: 1) the effects have never been reproduced since the initial publications of at least 10 years ago; 2) a very recent meta-analysis publication has shown that antioxidant vitamin supplementation increases mortality (Bjelakovic *et al.*, 2007), even though this review did not focus on the use of such supplements in the elderly population.

14.3.3 Overview

The numerous studies showing that micronutrient supplements enhance immune responses in the frail, and even in the apparently healthy elderly indicate that micronutrient deficits are detrimental to the immune responses, mainly CMI, of the elderly. The few studies that have shown clinical effects indicate that supplements may be beneficial, and this is of great importance since nutritional micronutrient deficits are quite common in the elderly population. Therefore, supplements of this kind for older adults have been advertised all over the world. These messages must be considered with great caution. Most of the advertised supplements have never been studied; and for the nutrient supplements that have been studied, it is still unclear what the appropriate doses are for elderly people in different states of health. In addition, supplements may be detrimental. It is far too early yet for recommendations about useful supplements for elderly people without any clear deficiency diseases. Even if many questions are still under investigation, it is nevertheless obvious that there is a need for micronutrient supplementation(s) for some elderly people, since micronutrient deficits are detrimental and also quite common. This was pointed out by the new French RDAs that raise the required levels for some micronutrients (Cynober *et al.*, 2000; Martin, 2001).

14.4 Immune responses in diseased, undernourished elderly: tertiary immune responses

Major undernutrition (protein-energy malnutrition or PEM) is a common disease in elderly populations. PEM prevalence has been reported to reach 2–4% in home-living, self-sufficient 75-year-old elderly (Dirren *et al.*, 1991; Lesourd *et al.*, 1996a; Lecerf *et al.*, 1989), and more than 50% in elderly hospitalized in acute care (Lesourd *et al.*, 1996b; Alix and Constans, 1998). Most PEM cases are related to chronic insufficient intake in the home-living elderly, while in hospital PEM results both from chronic insufficient intake and/or insufficient increases in intake during diseases (Lesourd, 1994; 1996). Indeed, when ongoing diseases are present, acute phase reactions are the indication of the metabolic changes that are occurring. Pro-inflammatory cytokines induce activation of defense mechanisms, but they also induce mobilization of the body's nutritional reserves (Lesourd *et al.*, 1996b). The latter metabolic changes could only be compensated by a period of increased intake (Lesourd and Mazari, 1997). In fact, pro-inflammatory-induced anorexia occurs in patients with age-related appetite dysregulation (Roberts *et al.*, 1994; Lesourd *et al.*, 2001), which in most cases, leads to chronic insufficient intake and PEM. It is very difficult for elderly patients to achieve sufficient intake during acute diseases, and therefore most acute diseases lead the elderly into PEM and PEM consequences (Lesourd, 1994; 1996).

The monocyte/macrophage cells which release pro-inflammatory cytokines, prompting reaction to acute disease, are of great importance for health status,

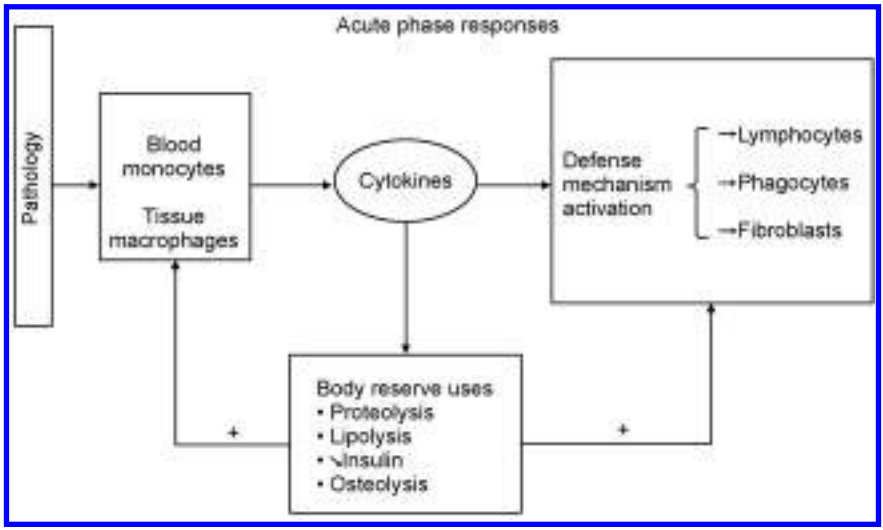

Fig. 14.2 Acute phase responses.

particularly in the elderly, since such responses may be detrimental. These cytokines induce activation of the body's defenses (e.g., lymphocytes and polymorphonuclears) and simultaneously induce the release of the body's nutritional reserves in order to provide activated cells with enough nutrients to combat ongoing disease (Lesourd, 1996; 1999; 2004) (Fig. 14.2). This cytokine-induced activation of the body's defense mechanisms is particularly dangerous in elderly patients for several reasons (Lesourd, 1996; 1999; 2004):

- the body's nutritional reserves are often at low levels, particularly in already undernourished patients exhibiting sarcopenia;
- during stress, the elderly need higher reserves since stress responses are of longer duration (Sapolski *et al.*, 1983);
- as protein synthesis is reduced after the age of 50 (Welle *et al.*, 1993; Yarasheski *et al.*, 1993; Boirie *et al.*, 1997), part of the body's protein reserves used to combat disease will never be rebuilt;
- age and stress induce changes in glucose metabolism, combining to cause important decreases in insulin secretion during acute phase responses (Paolisso *et al.*, 1995), then leading to hyperglycemia. This propels elderly people into a transient diabetic state when the acute disease is still ongoing, leading to more complicated therapy;
- the elderly use more of the body's nutritional reserves to face disease (Lesourd, 1996; 1999).

Indeed, the disequilibrium between lower CMI responses and preserved monocyte/macrophage functions leads to increased and long-lasting (Sapolski *et al.*, 1983) monocyte/macrophage cytokine secretions during acute diseases. This increase leads to a greater mobilization of the body's nutritional reserves (Lesourd, 1999; 2004; Lesourd *et al.*, 2002). Part of these nutritional reserves

Table 14.2 Functions of peripheral blood monocytes from elderly of different healthiness. Subjects were recruited using the SENIEUR protocol (apparently healthy) (Ligthardt *et al.*, 1994) or added criteria (very healthy) (Lesourd and Mazari, 1999) or being undernourished

	Very healthy young elderly n = 65	Apparently healthy young elderly n = 69	Undernourished self-sufficient young elderly n = 45
Age (years)	78.4 ± 5.7	78.1 ± 6.3	78.6 ± 6.4
Albumin ($g\,l^{-1}$)	42.4 ± 4.2	38.0 ± 3.7	31.2 ± 4.3***‡
C Reactive Protein ($mg\,l^{-1}$)	3.1 ± 1.4	7.6 ± 4.3*	15.8 ± 11.7**†
IL-1 production ($ng\,l^{-1}$)			
Spontaneous release	ND	ND	1.5 ± 1.5
Using 25 μg LPS for 10^6 $cells^{-1}$	2.8 ± 1.5	2.2 ± 1.9	1.3 ± 1.7
IL-1 production ($ng\,l^{-1}$)			
Spontaneous release	ND	0.1 ± 0.2	0.4 ± 0.2‡
Using 25 μg LPS for 10^6 $cells^{-1}$	1.9 ± 0.4	1.8 ± 0.5	1.0 ± 0.5***†

IL, interleukin
Significant differences from very healthy young elderly * $p < 0.05$, ** $p < 0.01$, ***$p < 0.001$
Significant differences from apparently young elderly † $p < 0.05$, ‡ $p < 0.01$
ND not detectable
LPS lipopolysaccahride

used will never be rebuilt, particularly the body's protein reserves, since protein catabolism is level in the aged population compared with younger adults, while protein muscle synthesis is lowered (Welle *et al.*, 1993; Yarasheski *et al.*, 1993). Any disease, therefore, causes the elderly to lower body protein reserves and subsequently leads to a higher degree of PEM.

In addition, PEM is associated with lower CMI responses, the degree of immunodeficiency being strongly related to the intensity of PEM (Lesourd, 1997; 1999; 2004; Lesourd *et al.*, 2002) (Table 14.2). When PEM is major, non-specific immunity is also decreased (Lesourd, 1997), leading to less efficient stress responses (Table 14.2). With disease after disease, the aged person consumes the body's nutritional reserves, mainly muscle proteins, until PEM appears. Response to further disease will then be less efficient and more prolonged, leading to a greater use of the body's nutritional reserves. With disease after disease, the body's nutritional reserves will be depleted, and when they are exhausted death will occur (Lesourd, 1996; 1997; 2004). The effect of PEM on immune responses is, therefore, particularly deleterious in the elderly.

It is difficult to effectively (re)feed elderly people who are suffering from PEM. It has been shown that CMI responses are restored during refeeding in elderly PEM subjects when the PEM is mild. This form of PEM is mainly due to chronic insufficient intakes (Lesourd, 1997; 1999; Lesourd and Mazari, 1997). In these patients, the restoration of the immune system is strongly correlated to the length of the refeeding therapy, when intakes are higher than 35 kcal/kg/d (Lesourd and Mazari, 1997; Lesourd, 1997). In contrast, when PEM is also

associated with acute phase responses (hypercatabolism), in spite of higher intakes (>40 kcal/kg/d), refeeding remains ineffective (Lesourd and Mazari, 1997) for a while. The therapy only becomes efficient for CMI responses when acute phase responses are decreased to quite low levels, i.e. when C reactive protein levels are lower than 30–40 mg/L (Lesourd and Mazari, 1997). This demonstrates that ongoing stress responses, which lead the patient to intensive use of the body's nutritional reserves, are difficult to combat in the elderly and may need very high levels of nutritional therapy. The energy supply should be at least greater than 35 kcal/kg/d (Lesourd and Mazari, 1997). The required levels of protein and other nutrients in refeeding therapy still remain in question, but they should at least meet the RDA for elderly people.

14.5 Conclusions

The link between immunity and nutritional status is strong, particularly in the aged population. The immune responses of elderly subjects are particularly sensitive to nutritional influences, not only in the case of major undernutrition (PEM), but also when micronutrient deficits occur. It is highly probable that the micronutrient needs of elderly subjects are higher than those of younger adults. The close relationship between micronutrient levels and CMI responses may be used to determine the required RDAs for the elderly. In addition, further studies are required to determine macronutrient needs during acute diseases in order to restore nutritional status (and immune responses). The efficiency of immune response when the body is challenged offers a promising way of quantifying the efficacy of nutritional therapy for healing.

14.6 References

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15

Nutrition and gut health in older people

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The intestinal microbes are most numerous in the large intestine. This organ, which is useful to mammals the food of which consists of rough bulky vegetable matter, and which require a large reservoir for the waste of the process of digestion, is certainly useless in the case of man.
Ilya Metchnikoff 1907 (*The prolongation of life*)

Abstract: At old age, intestinal function is reduced, while the requirement for nutrients is similar as for younger adults; also the sense of hunger and thirst is often impaired and may lead to under nutrition. The intestinal microbiota may play an important role here and has been suggested to be altered at old age. Specific functional foods containing prebiotics or probiotics may positively influence many of the intestinal dysfunctions observed, such as bowel and immune function. They may also positively affect nutritional status thereby contributing to a better quality of life.

Key words: probiotic, prebiotic, functional food, intestinal health, intestinal microbiota.

15.1 Introduction

Despite being often touted as the 'father' of probiotics, even Noble laureate Ilya Metchnikoff got it wrong in this case. Unlike what he suggested a century ago, the large intestine plays an important role in the health of humans too and is certainly *not* useless. Also in humans the intestine harbours a substantial microbiota that is involved in the degradation of fibre, i.e. Metchnikoff's 'rough bulky vegetable matter' (Metchnikoff 1907). Furthermore, the microbiota is involved in the production of vitamins, modulation of the immune system and protection from incoming (potential) pathogenic bacteria. The role of the

intestinal microbiota in these important functions is most clearly illustrated in so-called germ-free animals, which are animals raised without (intestinal) microbiota. Lacking the microbial stimuli required for the normal development of immune function, these animals have an immature immune system as adults. They also require substantially more energy than their microbiota-carrying counterparts, since they do not benefit from the energy salvaged by the intestinal microbiota through fermentation of fibre. Germ-free animals also need additional vitamins, such as vitamin K, which are otherwise produced by the microbiota (Norin and Midtvedt 2006).

The fermentation of fibre leads to the production of organic acids which, besides providing additional energy, also fulfil other physiological functions. Butyric acid has been shown to be important for maintenance of intestinal mucosal health (Scheppach and Weiler 2004). Organic acids in general will reduce the luminal pH and thereby improve the solubility of minerals such as calcium and magnesium and improve their passive absorption. The reduction in pH together with competition for nutrients and binding sites by the intestinal microbiota provides a protective mechanism referred to as colonisation resistance (Adlerberth *et al.* 2000), that reduces the ability of many (potential) pathogens to proliferate in the colon. Organic acids and the intestinal microbiota also play a role in bowel function (Ouwehand *et al.* 2005).

The large intestine provides an important habitat for the intestinal microbiota. This microbiota undergoes age-related changes during lifetime, due to changes in physiology and, especially in the elderly, due to shifts in feeding pattern, physical activity and, for example, the frequent use of medication. These changes in microbiota may affect intestinal health and general well-being.

15.2 Age-related changes in the gastrointestinal tract of the elderly

Ageing is associated with a decline in several body functions that can impact nutritional status (Brownie 2006). Typical physiological changes associated with ageing, include decreased lean body mass and bone density, increased proportion of body fat, and reduced physical activity and a decrease in basal metabolic rate and energy expenditure. Also psychological, social and financial barriers can contribute to decreased and insufficient energy intake. Consequently, the elderly are more vulnerable to malnutrition, especially individuals with chronic illnesses and medication. The nutritional status of elderly people is an important determinant of quality of life, morbidity and mortality (Brownie 2006; Gibbons and Henry 2005; Chernoff 2005). In the gut, malnourishment can lead to damage of the epithelial cells which in turn may cause a decrease in local immunity, reduced absorption of dietary components and loss of appetite. Furthermore, damaged epithelium may allow microbes of the intestine to translocate, thus, predisposing elderly to systemic infections and septicaemia (Hamilton-Miller 2005).

Table 15.1 Physiological changes in the gastrointestinal tract of elderly and their influence on gastrointestinal health and nutritional status

Organ	Changes in elderly	Effect
Smell and taste	Reduced smell and taste	Lack of appetite
Mouth	Tooth decay	Difficulty in chewing
Saliva	Decreased saliva secretion	Difficulty in swallowing
Esophagus	Decreased motility	Dysphagia
Stomach	Decreased gastric motility and flexibility	Delayed postprandial satiety
	Higher incidence of mutations of tumour suppressor genes	Gastric cancers
	Decreased gastric acid secretion	Malabsorption of nutrients, bacterial overgrowth in small intestine, reduced release of vitamin B_{12}
Pancreas	Minor decrease in secretion	Decreased response in metabolic stress
Gall bladder	Decrease in bile secretion	Decreased lipid absorption
Liver	Decrease in blood flow	Decreased elimination of toxins
Small intestine	Surface area decrease, no change in motility	Decreased absorption of lipids and sugars
Colon	Decreased motility	Constipation, diverticulosis?
	Higher incidence of mutations of tumour suppressor genes	Colon cancer

Although ageing has relatively little effect on the overall gastrointestinal function, the impaired adaptation to stress following injury or illness may cause malnutrition and gastrointestinal disorders of the aged patients (Woudstra and Thomson 2002). Age-related physiological changes of the gastrointestinal tract are shown in Table 15.1. However, physiological changes in the ageing gut may be difficult to differentiate from disease induced alterations (Dholakia *et al.* 2005).

Poor dentition can reduce the intake of fibrous foods (e.g., whole grain products, vegetables and fruits) that require mastication (Kremer *et al.* 2007, Russell *et al.* 1999). Reduction and alterations in smell and taste occur with advancing age, and impaired sensory perception can reduce appetite and the pleasure provided by a meal. Impaired taste and smell are also likely to reduce the cephalic phase of digestion; that is the salivary, gastric, pancreatic and intestinal secretions evolved to initiate digestion (Hays and Roberts 2006). Saliva protects the teeth, and lubricates the mouth facilitating chewing and swallowing. Although decreased salivary flow is common in older people (Ship 2002) it is mainly due to systemic diseases and medication rather than ageing itself (Gupta *et al.* 2006).

Increased prevalence of gastrointestinal reflux and constipation with increasing age are associated with impaired esophageal (Ferriolli *et al.* 1998) and colonic motility (Madsen and Graff 2004). The mechanisms behind the age-related motility changes are thought to be related to the degeneration of the

enteric nervous system (ENS) (Gabella 1989, Santer and Backer 1988). Especially the cholinergic neurons of the ENS have been found to be susceptible to neurodegeneration with age (Johnson *et al.* 1998). The degeneration of the ENS decreases also the gastric motility (Shimamoto *et al.* 2002). The delayed gastric emptying rate and the subsequent antral distension increases satiety and decreases hunger (Hays and Roberts 2006). Also a variety of gut hormones (glucagon, GLP-1, CCK, leptin, ghrelin and NPY), signalling peripheral satiety and hunger signals, are suggested to induce a less pronounced response at old age. This reduced response to satiety and hunger hormones indicates that elderly may lack the ability to compensate for over- and underfeeding periods (Hays and Roberts 2006).

The gut epithelium and its proliferation are important for the maintenance of the integrity of the gut lining. Although the epithelial stem cells maintain proliferation capacity throughout life, it seems that they show functional impairments and accumulation of histological damages with age (reviewed by Kirkwood 2004). The age-related increase in apoptotic responses to irradiation stress have been described mainly in murine intestine (Martin *et al.* 1998).

Reduced nutrient absorption of the small intestine is associated with both the morphological and functional changes with ageing. In studies with animals the surface area of jejunum has been observed to decrease with age (Keelan *et al.* 1985); however, this loss of the surface area can be compensated for by the ileum (Raul *et al.* 1988). In animal studies, the absorption rates of glucose and amino-acid are decreased with age (Vinardell 1987; 1992; Ferraris and Vinnakota 1993). Although age-associated decline in carbohydrate absorption has also been found in humans (Hosoda 1992, Feibush and Holt 1982), it may have minimal nutritional impact on elderly consuming a normal diet. However, bacterial overgrowth is common in elderly and may reduce the ability to absorb carbohydrates (Riepe *et al.* 1980). Lipid digestion and absorption are relatively well-preserved in ageing (Holt and Balint 1993). The malabsorption of lipids with ageing seems to be more related to the decreased intestinal surface area than the absorption itself (Woudstra *et al.* 2004a). Other mechanisms such as decreased bile secretion and consequent lipid solubilisation have been suggested (Holt and Balint 1993). Recently decreased fatty acid (FA) absorption was found to be associated with reduced intestinal FA-binding protein and ileal lipid-binding protein (Drozdowski and Thompson 2006; Woudstra *et al.* 2004b).

The micronutrients that are of particular concern in the elderly are calcium, vitamin D and vitamin B_{12} (Russell *et al.* 1999). Vitamin D insufficiency can be related to decreased sun exposure (Russell 2000), and calcium absorption decreases/declines in elderly are probably due to a concomitant decrease in D-vitamin receptors and availability in the small intestine (Nagar and Roberts 1999). B_{12} vitamin deficiency is commonly caused by malabsorption resulting from gastric dysfunction rather than dietary insufficiency (Dholakia *et al.* 2005). Gastric mucosa atrophy results in inadequate secretion of HCl, pepsinogen and intrinsic factor, which decreases the absorption of vitamin B_{12} from the intestine (Russell 2001). However, the major cause of gastric atrophy is not ageing, but a

Helicobacter pylori infection, which may affect over 50% of the elderly in many parts of the world. Also medication can reduce the acidity of the stomach and induce malabsorption of vitamin B_{12} (Wolters *et al.* 2004, Newton 2004). Additionally, the reduced acid secretion elevates the intestinal pH, which can lead to overgrowth of micro-organisms in the intestine and weaken the barrier protecting against intestinal translocation (Wolters *et al.* 2004) and further interfere with the absorption of micro- and macronutrients (Nagar and Roberts 1999). Pre- and probiotics obtained from the diet could be helpful by decreasing the luminal pH and enhancing the absorption of micronutrients (i.e. calcium and magnesium) (Scholz-Ahrens *et al.* 2007).

In addition to inadequate nutrition, elderly persons are prone to dehydration. Age-related alterations in kidney function may lead to hypotonic urea and enhanced water diuresis. In parallel, the thirst sensation is decreased, probably due to compromised activity of osmoreceptors. Decreased body water content due to physiological changes in body composition, and some medications that affect the fluid balance, may further aggravate the condition (Volkert *et al.* 2005).

15.3 Intestinal immune function of the elderly

The role of intestinal microbiota in development of immune responses has been demonstrated effectively by showing significant deficiency of maturation in the absence of intestinal microbes (Bauer *et al.* 2006). The interaction between the intestinal immune system and microbes is important for well-being and continues throughout life. Because the intestine is a lucrative gateway for pathogens to the body, the intestinal immune system has to learn to differentiate between pathogens and commensal bacteria. Furthermore, the ingested food is composed of structures that are by definition 'non-self' to the immune system and thus must be considered as something to potentially initiate immune response to. Therefore it is not surprising that the regulation of the intestinal immune system is different from that of the systemic responses. Great emphasis is put on reducing unnecessary responses, e.g. by the production of IgA which does not activate other arms of the mucosal immune system or secretion of transforming growth factor (TGF)-β, to down-regulate inflammatory responses and direct towards oral tolerance initiated immune functions (Fagarasan and Honjo 2003, Alpan 2001). Upon ageing, the composition of the intestinal microbiota as well as the immune responses change. The relationship between these concomitant changes is, however, poorly understood. Susceptibility to several diseases increases in the elderly and the observed general immune senescence can play a role also in the intestine in development of diseases like various intestinal cancers, inflammatory diseases, autoimmune diseases and diarrhoea (Hebuterne 2003, Caruso *et al.* 2004, Hasler and Zouali 2005, Lyytikäinen *et al.* 2007).

The changes in the immune system of the elderly appear complex with altered balance rather than mere deficiency of immune functions. Some

functions such as concentrations of circulating inflammatory markers are indeed enhanced in the elderly (Kritchevsky *et al.* 2005) but functions like the ability to respond to skin testing with delayed type hypersensitivity are weakened (Goodwin 1995). The effect of ageing on the intestinal immune function has been studied only to a limited extent.

The different arms of the immune system are affected differently. The cellular type immune responses are compromised most by age (Lesourd and Meaume 1994). The number of immune cells decrease in the mucosa when their movement from both blood and Peyer's patches is reduced and signalling between immune cells may be altered (Schmucker *et al.* 2001, Ogino *et al.* 2004, Hasler and Zouali 2005). Furthermore, the cytokine synthesis is altered. Antigen stimulated synthesis of interferon (IFN)-γ, the central regulatory cytokine for cell-mediated responses, is lacking in Peyer's patches of elderly (Fujihashi and McGhee 2004), whereas in the systemic response it can be increased (Ernst *et al.* 1995). Elderly reaching over 90 years of age may also suffer from a more profound reduction in T-cell function than younger seniors (Lesourd 2006).

Inflammatory biomarkers tend to increase in the blood with increasing age. In elderly over 65 years of age, serum concentrations of interleukin (IL)-6, IL-10 and tumour necrosis factor (TNF)-α may be increased and associated with increased incidence of cardiovascular disease (Kritchevsky *et al.* 2005). It has even been postulated that persons who maintain low inflammatory activity live longer (Bengmark 2006). In theory, due to reduced reactivity of immune cells to stimuli, the immune cells attempt to compensate by secreting more pro-inflammatory factors thus resulting in longer or increased pro-inflammatory responses with multiple side-effects in the body, such as, for example, increased muscle break-down (Lesourd 2006). This theory is supported by the finding that PGE_2 secretion by monocytes is increased by age. PGE_2 is a powerful immunosuppressant. However, in the intestine concentrations of PGE_2 appear to decrease with age therefore reducing gut motility and decreasing cytoprotection of the mucosa (Tiihonen *et al.* 2008b).

The decreased cellular immune functions lead to emphasis on antibody-associated responses in elderly. This can be demonstrated by increases in IgG and IgA concentrations in the serum, and saliva (Arranz *et al.* 1992, Lesourd *et al.* 1998, Meyer 2005). The faecal concentrations of IgA appear not be decreased (Arranz *et al.* 1992, Tiihonen *et al.* 2008b), although the migration of B-cells to the mucosa may be decreased (Schmucker *et al.* 2001). However, the antibody-associated responses can be further weakened due to the decreased T cell regulation of the humoral responses. The excess of antibodies in the blood appear to reflect increased autoimmunity to self antigens (Meyer 2005). Whereas, vaccination appears to be a less efficient way to improve immunity, e.g. against influenza in elderly than in young adults (Goodwin *et al.* 2006), also the intestinal responses may be weakened to oral challenge by pathogens or vaccination (Fujihashi *et al.* 2000).

Changes in the nutritional status may further impair the immune responses in the elderly (Mazari and Lesourd 1998). Especially specific micronutrients such

as vitamins A, B, C, and E, as well as iron, zinc, copper, magnesium and selenium play an important role. Vitamin E is perhaps the most studied micronutrient in relation to immune responses. The effect of vitamin E deficiency on the intestinal immune functions has not been well characterised in the elderly. The deficiency results in general in impaired cellular and humoral responses. Supplementation of diet by vitamin E has been shown to reduce respiratory infections in the elderly (Han and Meydani 1999, Meydani *et al.* 1997), although such a benefit was not observed by Graat and co-workers (2003).

15.4 Intestinal microbiota of the elderly

Human intestinal microbiota is known to have predominant effects on host health. Gut microbiota of healthy persons is generally very stable, but disease-, diet- and age-related changes in the microbiota are known to occur. Therefore, gut microbiota, which is thought to consists of some 10^{14} cells (Savage 1977), can be seen as a dynamic multi-cellular 'organ', the components of which actively interact with each other as well as with the host. It has been long recognised that the gut microbiota of elderly often differs from that of healthy adults. Altered gut microbiota may result from changes in the diet, which in turn may be caused by a number of reasons, including chewing and swallowing difficulties, decline in taste and smell, and masticatory dysfunction. Other reasons for altered gut microbiota of the elderly may include malnutrition, immunologic changes, hospitalisation, increased intestinal transit times and lack of physical activity, recurrent infections, and the use of antibiotics (Bartosch *et al.* 2004).

The intestinal microbiota in the elderly is thought to be more complex in composition than in adults (Blaut *et al.* 2006). The species harboring human gut microbiota have remained largely unknown and uncultured (Eckburg *et al.* 2005). Cultivation-based assays have yielded valuable information on the typical composition of gut microbiota over the years. However, as many species typical of the human intestinal microbiota are uncultivable by current laboratory procedures, cultivation-based studies have had their limitations in reflecting the composition of the microbiota. In the advent of molecular methods and high-throughput techniques, the analysis of complex microbial communities such as the gut microbiota has taken long strides forward. Using molecular methods, several groups have identified the components typical for the gut microbiota in the elderly. In these studies, the major components of the gut microbiota of the elderly have been identified as *Bacteroides* and relatives (4–20% of total bacteria) (Bartosch *et al.* 2004, Hayashi *et al.* 2003, He *et al.* 2003, Hold *et al.* 2007, Mueller *et al.* 2006), *Clostridium* rRNA subcluster XIVa (*C. coccoides* group; 3–20% of total bacteria) (Bartosch *et al.* 2004, Hayashi *et al.* 2003, Hold *et al.* 2007, Mueller *et al.* 2006), *Clostridium* rRNA cluster IV (*C. leptum* group) (Hayashi *et al.* 2003; Hold *et al.* 2007), and *Faecalibacterium* (Bartosch *et al.*

2004, Hayashi *et al.* 2003, He *et al.* 2003, Mueller *et al.* 2006). These results have been in accordance with earlier culture-independent assessments of the gut microbiota of healthy adults (Harmsen *et al.* 2002; Suau *et al.* 1999). Other suggested major groups of elderly microbiota include *Clostridium* rRNA cluster IX (Hayashi *et al.* 2003), genus *Bifidobacterium* (Bartosch *et al.* 2004, He *et al.* 2003), '*Gammaproteobacteria*' (Hayashi *et al.* 2003), *Ruminococcus* group (He *et al.* 2003), and *Atopobium* group (He *et al.* 2003).

A number of age-related changes in the gut microbiota have been suggested to occur in the elderly. While the total anaerobe counts appear to be relatively stable as the age increases (Woodmansey *et al.* 2004), changes in the genera and species composition have been reported. Compared to adults, the contribution of *Bacteroides* and *Clostridium coccoides* groups to the gut microbiota of the elderly is reduced (Bartosch *et al.* 2004; He *et al.* 2003; Woodmansey *et al.* 2004). Reduced levels of predominant carbohydrate digesters such as *Bacteroides* may have marked implications for the nutrition of the elderly (Bartosch *et al.* 2004), although it has been reported that faecal enzymatic activity and major metabolites resulting from carbohydrate fermentation are similar between different age groups (Andrieux *et al.* 2002). Changes in the levels of *Clostridium* may be species or cluster-specific; increased total *Clostridium* levels (Mitsuoka and Hayakawa 1972) and decreased levels of *C. coccoides* group (Hayashi *et al.* 2003) in the elderly have been reported. Notably, both the incidence and the severity of *C. difficile* infections are increasing, particularly in among the elderly (Lyytikäinen *et al.* 2007).

Elderly subjects may have higher incidence of *Enterobacteria* compared to healthy adults; 5–10% vs. 0–5% respectively (Gavini *et al.* 2001, He *et al.* 2003, Mueller *et al.* 2006). Elderly subjects may also have higher incidence of certain strains of *Klebsiella, Proteus* and *Providencia*, 5–10% vs. 0% respectively (Gavini *et al.* 2001). *Enterococcus*, *Ruminococcus* group and *Eubacterium cylindroides* group have also been reported to be higher in elderly subjects compared to adults (He *et al.* 2003). It has been suggested that, through the production of detrimental metabolic end-products, a rise in fusobacteria, propionibacteria, clostridia and other proteolytic bacteria observed in the elderly may indicate putrefaction of large bowel (Woodmansey 2007).

Increased levels of *Lactobacillus* in the elderly have been reported based on culture-dependent (Mitsuoka and Hayakawa 1972) and culture-independent assays (He *et al.* 2003). A number of *Lactobacillus* species has been isolated from elderly subjects. Silvi and others (2003) identified *L. fermentum* as the most prevalent species among healthy Italian elders, followed by *L. paracasei* subsp. *paracasei*, *L. acidophilus* and *L. plantarum*. Likotrafiti and others (2004) reported *L. casei* and *L. fermentum* as the most prevalent lactobacilli in elderly Italian subjects.

Altered gut microbiota of the elderly is partly due to hospitalisation and frequent antibiotic use rather than the age of the subjects as such. Bartosch and others (2004) reported significantly reduced levels of all eubacteria and

Bacteroides/*Prevotella* group, *Faecalibacterium prausnitzii*, and *Clostridium clostridiiforme* in hospitalised elderly subjects compared to healthy elderly subjects. Furthermore, in hospitalised elderly patients receiving antibiotic treatments, also genus *Bifidobacterium*, genus *Desulfovibrio*, and *Clostridium butyricum*, *Ruminococcus albus* and *Enterococcus faecalis* were reduced compared to healthy elderly. Similarly, the alterations in the gut microbiota reported by Hopkins and others (Hopkins *et al.* 2001; Hopkins and Macfarlane 2002) were much more significant in elderly subjects with *C. difficile* associated diarrhoea than in healthy elderly subjects. In addition, the area of living may affect the gut microbiota; differences between the gut microbiota of elderly living in rural and in urban areas have been reported (Benno *et al.* 1989). Such differences may be due to higher dietary fibre content in rural diets. Moreover, Mueller and others (2006) demonstrated that the age-related differences in the gut microbiota vary between different countries.

Genus *Bifidobacterium*, an important component of colonic microbiota, is of specific interest here, as bifidobacteria are thought to play a crucial role in gut health. Bifidobacteria have been linked with a number of health benefits (Crittenden 2004). Furthermore, aberrancies in *Bifidobacterium* microbiota have been linked with certain diseases (Kirjavainen *et al.* 2002). Several studies have indicated that compared to healthy adults, the levels of bifidobacteria are decreased in the elderly. Mutai and Tanaka (1987) reported average fecal *Bifidobacterium* levels of approximately 10^9 CFU/g in centenarians, compared to levels of 10^{10} CFU/g in other age groups. They also suggested that in the elderly, the ratio of non-anaerobes to anaerobes is much larger in the elderly than in adults. Lower levels of bifidobacteria based on culture-dependent assays have also been reported by other authors (Gavini *et al.* 2001, Mitsuoka and Hayakawa 1972, Mitsuoka and Kaneuchi 1977, Woodmansey *et al.* 2004). Conversely, He and others (2003) reported that bifidobacteria make up a higher proportion of the total faecal microbiota in the elderly compared to adults. One possible explanation for this difference between the studies is the methodology used: the earlier reports were based on culture-dependent assays, while He and others (2003) used culture-independent approach. Similarly, Hopkins and others (2001) reported that based on cultivation method, the levels of bifidobacteria in elderly were lower than in adults, but based on 16S rRNA quantification, such effect was not observed. It is possible that the age-related changes in *Bifidobacterium* microbiota are related to the culturability of the bacteria, which in turn is influenced by species composition and possibly also by the activity of the cells. Culture-based studies favour the species and strains which are readily cultivable in laboratory conditions. In addition, minor components of the microbiota are easily overlooked by culture methods, as these species are overgrown by closely related dominant species.

Age-related changes in *Bifidobacterium* microbiota may be largely due to changes in the species composition and diversity, rather than changes in the total level of the genus (Hopkins and Macfarlane 2002). Several studies have focused on the species composition of the elderly's *Bifidobacterium* microbiota.

Studying Japanese centenarians, Mutai and Tanaka (1987) concluded that the most prevalent species of *Bifidobacterium* in the elderly are *B. adolescentis* and *B. bifidum*. Other studies have suggested *B. adolescentis* and *B. longum* as the two dominant faecal species of *Bifidobacterium* in the elderly (Gavini *et al.* 2001, He *et al.* 2001, Silvi *et al.* 2003), while Woodmansey and others (2004) identified *B. angulatum* as the predominant species. Conversely, based on 16S rDNA sequencing, Likotrafiti and others (2004) identified the majority of *Bifidobacterium* isolates from elderly subjects being closely related to *B. infantis*, although others have suggested that *B. infantis* occurs solely in infants and babies (Mangin *et al.* 1999). *B. breve* is also prevalent in infants, but rarely detected in adults or elderly (Gavini *et al.* 2001). *B. dentium* is occasionally isolated from faecal microbiota of the elderly, albeit at low levels (Gavini *et al.* 2001). Gavini and others (2001) detected *B. bifidum* in 17% of elderly French subjects, while the prevalence of this strain in Japanese elderly subjects is higher according to Matsuki and others (1999) (38%) and Mutai and Tanaka (1987) (43%). In Italian subjects, the frequency of *B. bifidum* was 33%, as reported by Silvi and others (2003).

Other than the composition of the microbiota, also the functionality and the activity of the gut microbiota components may undergo age-related changes. For example, adhesion properties of beneficial bacteria to host intestinal contents such as mucus and intestinal epithelial cells may be age-dependent. The adhesion capacity of bifidobacteria isolated from elderly subjects has been reported to be inferior to that of bifidobacteria isolated from adults (He *et al.* 2001). On the other hand, bifidobacteria appear to bind more effectively to mucus isolated from infants and adults, compared to mucus isolated from elderly (Ouwehand *et al.* 1999).

In conclusion, the intestinal microbiota of the elderly is dominated by *Bacteroides* and relatives, *Clostridium coccoides* and *C. leptum* groups, and *Faecalibacterium*, Table 15.2. The main components of the intestinal microbiota of the elderly are similar to that of adult microbiota, but age-related changes in the levels of the dominant and less dominant microbial groups do occur. It is well-established that ageing is linked with reduced total levels of readily cultivable total bifidobacteria; however, the evidence from culture-independent studies is less clear. Nevertheless, age-related differences in the species composition of bifidobacteria are well-demonstrated.

Despite the well-established differences in microbiota composition between adults and seniors; the causal relation between age, physiological changes and changes in microbiota composition are not well understood. Therefore, also the implications of the change in microbiota composition are currently not clear.

15.5 Functional foods for the elderly

As mentioned above, elderly subjects have specific nutritional needs, e.g. due to their altered physiology. Furthermore, the composition and activity of their

Table 15.2 Suggested major bacterial groups of the intestinal microbiota of the elderly

Group	Reference
Bacteroides and relatives	Bartosch *et al.* (2004); Hayashi *et al.* (2003); He *et al.* (2003); Hold *et al.* (2007); Mueller *et al.* (2006)
Clostridium rRNA subcluster XIVa (*C. coccoides-Eubacterium rectale* group)	Bartosch *et al.* (2004); Hayashi *et al.* (2003); Hold *et al.* (2007); Mueller *et al.* (2006)
Clostridium rRNA subcluster IV (*C. leptum* group)	Hayashi *et al.* (2003); Hold *et al.* (2007)
Clostridium rRNA cluster IX	Hayashi *et al.* (2003)
Faecalibacterium	Bartosch *et al.* (2004); Hayashi *et al.* (2003); He *et al.* (2003); Mueller *et al.* (2006)
Bifidobacterium	Bartosch *et al.* (2004); He *et al.* (2003)
Gammaproteobacteria	Hayashi *et al.* (2003)
Ruminococcus group	He *et al.* (2003)
Atopobium group	He *et al.* (2003)

intestinal microbiota differs from younger adults and their immune function may be reduced. Nutritional strategies can be designed to fulfil these needs and improve those functions.

15.5.1 Modulation of microbiota composition and activity

Differences in the composition and activity of the intestinal microbiota of elderly as compared to younger adults maybe due to various reasons; changes in physiology, feeding pattern, physical activity and use of medication (disease). It may not always be possible to reverse these changes. Therefore, other methods for compensating these microbiota disturbing events can be considered. Consumption of foods or dietary supplements containing pre- and/or probiotics is the most commonly used approach, not only in the elderly but also in other age groups.

Probiotics were defined by a FAO/WHO work group as 'Live micro-organisms which when administered in adequate amounts confer a health benefit on the host' (FAO/WHO 2002). Probiotics, usually members of the genera *Lactobacillus* and *Bifidobacterium*, may influence the composition and/or activity of the intestinal microbiota. This is, however, not a prerequisite. Probiotics may also exert health benefits by, e.g. directly influencing the immune system of the host without any measurable change in microbiota activity or composition. Probiotics have many suggested health benefits (Table 15.3). Some are better documented than others. It is also important to note that each probiotic strain has specific health benefits which cannot be extrapolated to other strains, not even from the same species.

Table 15.3 Examples of proposed health benefits of selected probiotics and prebiotics, with special reference to the elderly

Health benefits	Example strains	References
Probiotics		
Improved bowel function	*Propionibacterium freudenreichii* JS + *Lactobacillus acidophilus* Lc705, *Bifidobacterium longum* 46 and 2C	Ouwehand *et al.* (2002), Pitkälä *et al.* (2007)
Reduced diarrhoea	*Lactobacillus casei* DN-114 001	Hickson *et al.* (2007), Plummer *et al.* (2004)
Improved innate immunity	*Lactobacillus rhamnosus* HN001, *Bifidobacterium lactis* HN019	Gill and Rutherfurd (2001), Gill *et al.* (2001)
Change in microbiota composition	*Bifidobacterium lactis* HN019	Ahmed *et al.* (2007)
Prebiotics		
Improved calcium absorption	Galacto-oligosaccharides, Fructo-oligosaccharides, Inulin + Oligo-fructose	van den Heuvel *et al.* (2000), Tahiri *et al.* (2003), Holloway *et al.* (2007)
Increased faecal *Bifidobacterium* levels	Inulin + Oligo-fructose, Inulin, Lactose	Langlands *et al.* (2004), Kleessen et al. (1997)
Improved bowel function	Lactitol, Lactulose, Galacto-oligosaccharides, Inulin	Rajala *et al.* (1988), Petticrew *et al.* (1997), Teuri *et al.* (1998), Kleessen *et al.* (1997)

Clostridium difficile is a common cause of diarrhoea in elderly subjects. Consumption of probiotics (*Lactobacillus acidophilus* and *Bifidobacterium bifidum*, strains not indicated) has been shown to reduce the symptoms of *C. difficile* infection and the levels of faecal toxins in elderly (Plummer *et al.* 2004). *Lactobacillus casei* DN-114 001 has been shown to reduce the incidence of antibiotic associated diarrhoea in elderly (Hickson *et al.* 2007). Consumption of probiotics has also been found to cause changes in faecal microbiota in elderly, e.g. consumption of *B. lactis* HN019 caused an increase in faecal levels of bifidobacteria, lactobacilli and enterococci, while enterobacteria were reduced (Ahmed *et al.* 2007). Since the microbiota of elderly subjects differs from that of younger adults, it may be important to select for probiotics for this particular age group (Laine *et al.* 2003). This is also indicated by the fact that probiotic bifidobacteria adhered to intestinal mucus *in vitro* in an age dependent manner (Ouwehand *et al.* 1999).

Prebiotics have been defined as 'Non-digestible food ingredients that, when consumed in sufficient amounts, selectively stimulate the growth and/or activity of one or a limited number of microbes in the colon resulting in documented

health benefits' (Ouwehand *et al.* 2006). Most prebiotics are oligosaccharides, although sugar alcohols and other modified carbohydrates are sometimes also considered prebiotics (Drakoularakou *et al.* 2007). Dietary fibre has many properties in common with prebiotics and the two terms are often used interchangeable. Prebiotics and fibre are, however, not the same. Both are not digested by human gastro-intestinal enzymes and are not absorbed in the gastro-intestinal tract. But, prebiotics are fermented selectively in the colon and exert their health effects via the colonic microbiota. Dietary fibre, on the other hand, may be fermented by a wider range of colonic microbes or is not fermented at all and may exert health benefits in other ways (e.g., through faecal bulking) (Ouwehand *et al.* 2006).

Subjects (31–81 years) consuming a mixture of 7.5 g oligofructose and 7.5 g inulin were found to have increased levels of mucosa associated bifidobacteria, eubacteria and lactobacilli in the proximal and distal colons while levels of clostridia, *Bacteroides* and coliforms were not affected (Langlands *et al.* 2004). Inulin alone, though at a high dose (40 g/day) was found to increase the levels of bifidobacteria and reduce the levels of faecal enterococci, while lactose (40 g/d) increased bifidobacteria and enterococci and reduced faecal levels of lactobacilli and clostridia in elderly subjects (68–89 years). No effect was, however, noted on the microbial activity in terms of faecal enzyme activity, lactate and short chain fatty acid levels (Kleessen *et al.* 1997).

Of course, probiotics and prebiotics can be combined to synbiotics; 'mixtures of pro- and prebiotics, which beneficially affect the host, by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract' (Gibson and Roberfroid 1995). Synbiotics are, however, much more than just a mixture of pro- and prebiotics. The prebiotic used should be a specific substrate for the selected probiotic, being able to stimulate its growth and/or activity while at the same time enhancing indigenous beneficial bacteria. The term synbiotic would suggest a synergy between the two components. It is, however, not clear whether this can always be obtained (Ouwehand *et al.* 2007).

Consumption of a combination of *Bifidobacterium lactis* Bb-01, *Bifidobacterium bifidum* Bb-02 and oligofructose-enriched inulin by healthy elderly volunteers led to higher levels of total faecal lactobacilli and bifidobacteria as compared to the placebo group. The species *B. lactis* and *B. bifidum* were detected at higher levels then in the placebo group (Bartosch *et al.* 2005). The study does not indicate, however, whether there was a synergy between the probiotic and prebiotic components. The administration of *Lactobacillus paracasei* ssp. *paracasei* F19 and inulin has been reported to increase the levels of faecal lactobacilli, but not bifidobacteria, in elderly subjects (Sullivan *et al.* 2001), while administration of *B. lactis* HN019 combined with galacto-oligosaccharides resulted in increased levels of both lactobacilli and bifidobacteria (Gopal *et al.* 2003).

Although many studies indicate that specific prebiotic, probiotics and synbiotics may be able to alter the composition of the intestinal (or rather faecal)

microbiota in many age groups, not only elderly, it should be noted that this is not a health benefit *per se*. A change in microbiota composition, often expressed as an increase in *Bifidobacterium* levels, can only be considered as an indicator for a healthy intestinal environment, but does not indicate health as such, nor is it a health benefit in itself.

15.5.2 Effect on bowel function

The most common gastrointestinal problem among elderly is certainly constipation. Lack of fluid can contribute significantly to constipation, as well as low intake of foods high in fibre (Russell *et al.* 1999). Also an altered composition of the colonic microbiota and the short chain fatty acids produced by the microbes correlate with changes in the intestinal motility (Hamilton-Miller 2005). Some probiotic strains and prebiotics have been shown to relieve constipation in elderly.

Healthy elderly subjects consuming fermented milk containing *B. lactis* DN-173 010 for two weeks, reported a significantly reduced oro-feacal transit times, and the positive effect lasted for two to six weeks after consumption of the probiotic was stopped (Meance *et al.* 2003). In frail elderly subjects, the consumption of fermented oat drinks with *B. lactis* Bb-12 or *B. longum* strains 46 and 2C resulted in normalized bowel movements (Pitkälä *et al.* 2007). Similar results of increased defecation in institutionalised elderly subjects were seen in four-week feeding trial with *L. rhamnosus* LC705 and *Propionibacterium freudenreichii* (subsp. *shermanii* JS) containing juice. However, no reduction in laxative use was observed (Ouwehand *et al.* 2002). These effects of probiotics on constipation may be strain specific (Fernández-Bañanes 2006).

Prebiotic compounds such as lactitol, fructo- (FOS), iso-malto- (IMO) and galacto-oligosaccharides (GOS), and inulin can act as substrates for probiotics and encourage their growth in the intestine, thus effecting constipation (Fernández-Bañanes 2006; Hamilton-Miller 2005). In constipated, elderly patients, inulin from chicory (20 to 40 g per day) had a moderate laxative effect, relieving constipation (Kleessen *et al.* 1997). GOS supplemented yoghurt (9 g per day), increased defecation frequency in two-week cross-over study with constipated elderly women (Teuri and Korpela 1998) and IMO consumption (10 g) for 30 days improved bowel movement and stool output in elderly male subjects. Also a significantly increased fecal acetate and propionate levels were observed after IMO supplementation together with the functional benefits (Chen *et al.* 2001). Lactitol has an effect on constipation through promoting the hydration of the gut contents, resulting in shorter transit times (Ouwehand *et al.* 2007). In elderly, lactitol (together with guar gum and wheat bran in yoghurt) has been shown to increase the faecal output (Rajala *et al.* 1988). Research results therefore suggest that in general prebiotics appear to be more effective in improving bowel function than probiotics, Table 15.3.

Increased intake of dietary fibre, especially insoluble non-starch polysaccharides, has been shown to relieve constipation in several studies. Dietary

fibre acts in a slightly different way than prebiotics; insoluble non-starch polysaccharides increase effectively faecal bulk whereas soluble non-starch polysaccharides bind water to the bulk. Resistant starch, which is not digested in small intestine, is unselectively fermented by the colonic microbes increasing the short chain fatty acids and gut motility (reviewed by Topping 2007).

15.5.3 Modulation of immune status

Different strategies have been applied for improving the immune status of elderly with nutrient supplementation. Selection of subjects has proven to be an important factor for successful intervention. Selection can be done according to age, health status, or nutritional status. Firstly, it appears that seniors over 70 would model a situation where less individual variation in the ageing process is present and thus smaller numbers of subjects can be analysed. Secondly, the health status is decisive. Subjects with excellent health may exhibit an immune status not different from young adults. Furthermore, an underlying disease may have such devastating effects on the immune functions that supplementation with nutrients is unlikely to improve the prognosis. Thirdly, deficiency in micronutrients can cause problems in immune functions, and selection of subjects with particular deficiencies can help to show improvement by dietary supplementation (Meydani *et al.* 2005). Unfortunately there is only scarce epidemiological information available of the effect of age, health status or micronutrient status on immune functions. Thus, more studies are needed that have sufficient background information available, as well as studies with pre-screened or selected subjects. When intestinal immune function is studied, pre-selection of subjects with altered balance of microbiota, or subjects with low number of lactic acid bacteria may be of importance (Tiihonen *et al.* 2008a).

In the following considerations, the effect that micronutrients may have on the intestinal immune responses is not included. The emphasis is put on the effects of pro- and prebiotics that have been shown to modulate intestinal immune function. Probiotic bacteria can, for example, function as adjuvants improving specific intestinal antibody responses (e.g., Fukushima *et al.* 1998, Link-Amster *et al.* 1994) and prebiotics in combination with probiotics or on their own, can increase intestinal antibody responses as well (e.g., Roller *et al.* 2004, Peuranen *et al.* 2004).

In most cases, the effects of mostly probiotics have been studied focusing on systemic immune responses. A rare clinical study with emphasis on local immune responses in the small intestine was conducted with patients undergoing resection of a short segment of the small bowel. Twenty-two patients were included in this study. The age range in the group receiving probiotics was 42–78 years, and in the control group it was 28–79 years. The patients received a probiotic drink containing approximately 2×10^{10} CFU/day *Lactobacillus plantarum* 299v supplementation for a median of nine days duration prior to surgery. Tissue sections were obtained during surgery, and numbers of plasma cells and IgM positive cells in lamina propria, and amount of IgA and IgM on

the mucosa were evaluated. Higher numbers of IgM positive cells were found in the mucosal surface in the control group. The significance of this finding is unclear. No other differences were detected. It is noteworthy that individual variation could not be taken into account, thus baseline levels may have been different in the two groups although the groups did not differ in the recorded demographic details (Woodcock *et al.* 2004).

In another study, the effect of combination of a probiotic and a prebiotic product were assessed by supplementing the diet for one year by daily nutritional formula containing vitamin E, B_{12}, folic acid, *Lactobacillus paracasei* NCC 2461 (10^9 CFU) and fructo-oligosaccharide (6 g) (Bunout *et al.* 2004). The mean ages of the subjects were 74 ($n = 30$) in the supplemented, and 75 ($n = 30$) years in the control group. Differences in the systemic immune status were detected, such as decreased baseline NK activity in the supplemented group. Both groups responded similarly to influenza and pneumococcal vaccination. However, significant differences were reported in the respiratory, gastro-intestinal, skin, genito-urinary infection rates. The supplemented group reported fewer infections, especially respiratory infections during the study period. The importance of each ingredient in the supplement was not assessed separately. Gastro-intestinal immune functions were not addressed.

Turchet and co-workers (2003) supplemented the diet of elderly subjects with *Lactobacillus casei* DN-114 001 for three weeks. This did not reduce the frequency of respiratory or gastro-intestinal infections but reduced the duration of the illness significantly.

Ex vivo NK cell activity and phagocytic activity of mononuclear and polymorphonuclear phagocytes were found to be increased after consumption of *Bifidobacterium lactis* HN019 by healthy elderly volunteers (Gill *et al.* 2001). Similar observations were made after consumption of *Lactobacillus rhamnosus* HN001 by health elderly volunteers (Gill and Rutherfurd, 2001). Gastro-intestinal immune functions were not addressed for either of the strains.

15.6 Future trends

Intestinal health has been one of the main focus areas of probiotic and prebiotic functional food ingredients. With the ageing of the general population in Western countries, it is certain that intestinal health of elderly subjects will receive more attention. In addition to fundamental research in this area, it is likely that more research will be done in the development of functional foods and supplements for this age group. In the future, we can expect an expansion of our knowledge on the ageing intestine, its microbiota, and products aimed at maintaining their health and adapted to their changing functionality. The marketing of such products will remain a challenge, as foods for elderly are not likely to be ‘sexy’ enough to attract the target customer since it confirms old age with all its accompanying inconveniences.

15.7 Sources of further information and advice

Further information on intestinal health and well being for different age groups can be obtained from a number of sources. Table 15.4 provides a list of examples. The list does not pretend to be complete, but gives a first hint on where to go for more in depth or more specific information.

Table 15.4 Examples of sources of further information

Topic	Source	Comment
Pre- and probiotics	www.isapp.net	The International Scientific Association for Probiotics and Prebiotics is an independent society that promotes the knowledge on these two functional food ingredients
Gastrointestinal microbiology	Ouwehand and Vaughan (2006)	Handbook on gastrointestinal microbiology
Intestinal microbiota	www.crownalife.be	Home page of EU funded project on intestinal microbiota of elderly
Legal issues	www.efsa.eu	European Food Safety Authority home page for information on legal matters concerning functional foods
Probiotics	www.howaru.com www.actimel.com www.yakulteurope.com	Company home pages on probiotic products
Prebiotics	www.litesse.com www.beneo.com	Company home pages on prebiotic products

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16

Nutrition and eye-related disorders

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Abstract: Age-related cataract and age-related macular degeneration (AMD) are the major causes of visual impairment and blindness in the aging population. There is much interest in the prevention of these two age-related eye diseases. Of particular interest is the possibility that certain dietary components intervention might reduce the incidence or retard the progression of these diseases. The nutrients that may be important in the prevention of these eye diseases are vitamins C and E and the carotenoids, lutein and zeaxanthin, zinc, and omega-3 fatty acids. There is biological plausibility to support a role of these dietary components in the protection of the lens and macula from light damage. Further support comes from epidemiologic studies evaluating dietary intakes and risk of these eye diseases.

Key words: cataract, age-related macular degeneration, vitamins C, vitamin E, lutein zeaxanthin, zinc, omega-3 fatty acids.

16.1 Introduction

Age-related cataract and age-related macular degeneration (AMD) are the major causes of visual impairment and blindness in the aging population. Approximately 50% of the 30–50 million cases of blindness worldwide result from unoperated cataract (Thylefors *et al.*, 1995; WHO, 1991; Schwab, 1990). A clinically significant cataract is present in about 5% of Caucasian Americans aged 52–64 yrs and rises to 46% in those aged 75–85 yrs (Kahn *et al.*, 1977). Cataract extraction is the most common surgical procedure performed in Medicare beneficiaries in the US (Javitt, 1993). This procedure is costly, accounting for 12% of the Medicare budget and accounts for more than $3 billion in annual health expenditures (Javitt, 1993; Steinberg *et al.*, 1993). For

these reasons, there is much interest in the prevention of cataracts. The prevalence of AMD also increases dramatically with age. Nearly 30% of Americans over the age of 75 have early signs AMD and 7% have late stage disease, whereas the prevalence among people 43–54 yrs are 8 and 0.1%, respectively (Klein *et al.*, 1992; Leibowitz *et al.*, 1980). AMD is the leading cause of blindness among the elderly in industrialized countries (Klein *et al.*, 1992; Counil NAE, 1984). Because there are currently no effective treatment strategies for most patients with AMD, attention has focused on efforts to stop the progression of the disease or to prevent the damage leading to this condition (Snodderly, 1995).

Cataract and AMD share common modifiable risk factors, such as light exposure and smoking (Snodderly, 1995; Taylor, 1999). Of particular interest is the possibility that certain dietary component intervention might reduce the incidence or retard the progression of these diseases. The nutrients that may be important in the prevention of these eye diseases are vitamins C and E and the carotenoids, lutein and zeaxanthin, zinc, and omega-3 fatty acids. Given that the lens and retina suffer oxidative damage, some of these nutrients are thought to be protective through their role as antioxidants. Additionally, lutein and zeaxanthin may provide protection as filters against light damage, i.e. absorbers of blue light and omega-3 fatty acids may provide anti-inflammatory effects.

16.2 Etiology of cataracts and age-related macular degeneration (AMD)

The role of the lens is to transmit and focus light on the retina. Therefore, for optimal performance the lens must be transparent. The lens comprises primarily water and protein. Normally, the protein is organized in such a way as to allow light to pass through the lens. Cataracts result when certain events, e.g. light exposure, cause a loss of this order and results in abrupt fluctuations in refractive index causing increased light scattering and loss in transparency in the lens. Increased lens opacity is thought to result from damage to lens enzymes, proteins and membranes by activated oxygen species, e.g. hydrogen peroxide, superoxide anion, and hydroxyl free radicals, which are formed from exposure to light and other types of radiation. Dietary antioxidants may be important in preventing this damage and, therefore, preventing cataracts.

AMD is a disease affecting the central area of the retina (Zarbin, 2004) resulting in loss of central vision. In the early stages of the disease, lipid material accumulates in deposits underneath the retinal pigment epithelium (Zarbin, 2004). This is proposed to occur after the RPE fails to perform its digestive function adequately. These lipid deposits (drusen) can be seen as pale yellow spots on the retina. The pigment of the RPE may become disturbed with areas of hyperpigmentation and hypopigmentation. AS AMD progresses, the RPE may atrophy completely. In some cases, new blood vessels grow under the RPE and into the subretinal space (exudative or neovascular AMD). If hemorrhaging

occurs, it can result in increased scarring of the retina. The early stages of AMD are in general asymptomatic. In the later stages there may be considerable distortion or complete loss of vision, particularly in the central area of vision (Snodderly, 1995). The specific pathogenesis of AMD is not known, although chemical- and light-induced oxidative damage to the photoreceptors is thought to be involved in the dysfunction of the RPE. The retina is particularly susceptible to oxidative stress because of its high consumption of oxygen, its high proportion of polyunsaturated fatty acids, and its exposure to visible light. Currently, there is no treatment which can restore vision in AMD. Therefore, efforts have focused on its prevention. As with cataracts, nutritional intervention has been suggested to play an important role in the prevention of AMD.

The antioxidants, vitamins C and E, lutein and zeaxanthin are common components of our diet that are most often implicated as protective against eye disease. These antioxidants may prevent damage in the lens by reacting with free radicals produced in the process of light absorption. Photoreceptors in the retina are subject to oxidative stress throughout life due to combined exposure to light and oxygen.

Vitamin E and carotenoids are lipid soluble oxidant scavengers that protect biomembranes. Vitamin C is an important water-soluble antioxidant and also promotes the regeneration of vitamin E. Both vitamins C and E are found in the lens (Yeum *et al.*, 1995; 1999; Taylor *et al.*, 1991). Of the 20–30 carotenoids found in human blood and tissues (Parker, 1989) only lutein and zeaxanthin are found in the lens and retina (Yeum *et al.*, 1999; Bone *et al.*, 1985). Lutein and zeaxanthin are concentrated in the macula or central region of the retina and are referred to as macular pigment. In addition to their role as antioxidants, lutein and zeaxanthin are believed to limit retinal oxidative damage by absorbing incoming blue light and/or quenching reactive oxygen species. Many putative risk-factors for AMD have been linked to a lack of macular pigment, including female gender, lens density, smoking, light iris color, and reduced visual sensitivity (Snodderly, 1995). Omega-3 fatty acids and zinc are highly concentrated in the retina and have been implicated in eye health.

16.3 Dietary intake and blood levels of nutrients and eye disease

16.3.1 Cataract

Vitamin C

Several studies have found a relationship between increased dietary vitamin C and decreased risk of cataract (Mares-Perlman *et al.*, 1995a; Jacques and Chylack, 1991; Leske *et al.*, 1991). It was observed that the prevalence of nuclear cataract was lower for men with total vitamin C intakes in the highest quintile category (104 mg/d) relative to the lowest intake quintile (33 mg/d) (Mares-Perlman *et al.*, 1995a). It has also been reported that the prevalence of cataract was about 75% lower in persons with vitamin C intakes >490 mg/day

that in those with intakes <125 mg/day (Jacques and Chylack, 1991). However, this relationship was not always observed (Hankinson *et al.*, 1992; Tavani *et al.*, 1996; Vitale *et al.*, 1993; The Italian-American Cataract Study Group, 1991).

Serum ascorbic acid level have been reported to be inversely associated with prevalence of cataract (Mares-Perlman *et al.*, 1995b; Simon and Hudes, 1999). However, Vitale *et al.* (1993) observed that plasma vitamin C concentrations were not associated with risk of nuclear or cortical cataract and one study found an increased prevalence of cataract with increased plasma vitamin C (Mohan *et al.*, 1989).

In a cross-sectional study investigating the relationship between plasma concentrations of antioxidants and nuclear, cortical, and posterior subcapsular cataracts in a group of men and women ($n = 372$, 66–75 years), high plasma concentration of vitamin C was not associated with decreased risk (Gale *et al.*, 2001).

Vitamin E

A protective effect of dietary vitamin E from cataract has been observed in several studies. Persons in the highest quintile for vitamin E intake were reported to be 50% less likely to undergo cataract extraction compared to those in the lowest quintile for vitamin E intake (Tavani *et al.*, 1996). Dietary vitamin E levels were not reported in this study. In addition, it has been reported that persons with vitamin E intakes in the highest quintile category had an approximately 40% lower prevalence of cataract relative to persons with intakes in the lowest quintile category (Leske *et al.*, 1991). However, others have (Jacques and Chylack, 1991) reported that although persons with vitamin E intake greater than 35.7 mg/d had a 55% lower prevalence of cataract than did persons with intakes less than 8.4 mg/d, this difference was not significant. Two other studies also reported no difference in cataract prevalence between persons with high and low vitamin E intake (Marles-Perlman *et al.*, 1995a; Hankinson *et al.*, 1992). However, in both of these studies, the null relationship was in women only. In the first study, dietary vitamin E was protective in men. In the second study only women were studied.

As with dietary vitamin E, results from studies reporting relationships between plasma vitamin E and cataract are inconsistent. Five studies examining this relationship have reported increased plasma vitamin E to be protective against the risk of cortical and nuclear cataracts (Vitale *et al.*, 1993; Leske *et al.*, 1995; 1998; Rouhiainen *et al.*, 1996; Knekt *et al.*, 1992). However, two studies observed that the prevalence of cataract was not related to plasma vitamin E concentrations (Vitale *et al.*, 1993; The Italian-American Cataract Study Group, 1991). In a cross-sectional study investigating the relationship between plasma concentrations of antioxidant vitamins and carotenoids and nuclear, cortical, and posterior subcapsular cataracts in a group of men and women ($n = 372$, 66–75 years), high plasma concentrations of vitamin E was not associated with decreased risk (Gale *et al.*, 2001). In contrast, in a sub-study of the Nutritional Factors in Eye Disease Study of Beaver Dam it was reported that there was a

significantly increased prevalence of nuclear cataract among 400 women and men (50 to 84 years) in the highest serum vitamin E quintile relative to those in the lowest quintile in (Marles-Perlman *et al.*, 1995a). Higher levels of α-tocopherol in the serum was not associated with less severe nuclear or cortical opacities overall. The authors suggest that the direct association with serum α-tocopherol in cross-sectional analyses may be the result of temporal confounding, which could occur if older or less healthy people improved their diets such that nutrient status at baseline examinations did not reflect the exposures that preceded the onset or progression of nuclear opacities. This was similar to the observation in the Baltimore Longitudinal Study on Aging (Vitale *et al.*, 1993) in which plasma α-tocopherol concentrations were significantly association with nuclear opacities in patients who had plasma concentrations measured 2–4 years before assessment of the lens (highest quintile adjusted OR: 0.5; 95% CI 0.3–1.0), but associations were not as storp for patients whose plasma samples were collected concurrent with eye examination (highest quintile adjusted OR: 0.8; 95% CI: 0.3–1.9).

Lutein and zeaxanthin

Although the data are few, studies suggest that dietary lutein and zeaxanthin play a role in cataract prevention. Berendschot *et al.* (2002) evaluated relationships between macular pigment optical density, i.e. macular lutein and zeaxanthin, and lens optical density in 366 subjects, aged 18–74 years. The lens optical density showed a significant association with macular pigment optical density ($p < 0.02$). The authors concluded that the inverse relationship between lens optical density and macular pigment optical density suggest that lutein and zeaxanthin may retard aging of the lens. Chasen-Taber *et al.* (1999a) observed in a prospective cohort of women from the Nurses' Health Study that those with the highest 10% of intake of lutein and zeaxanthin (13.7 mg/d) had a 22% decreased risk of cataract extraction compared with those in the lowest quintile (1.2 mg/d). Brown *et al.* (1999) also observed that there was a lower risk of cataract extraction in men with intakes of lutein and zeaxanthin but not other carotenoids. Men in the highest quintile of lutein and zeaxanthin intake (6.9 mg/d) had a 19% lower risk of cataract relative to men in the lowest fifth (1.3 mg/d) (95% CI:0.62, 0.98, P for trend = 0.01). There was no association with the other carotenoids. Mares-Perlman *et al.* (1994; 1995a) observed in women a significant inverse trend across quintiles of lutein intake. Women in the highest quintile of lutein intake (0.95 mg/d) had a 27% lower prevalence of nuclear cataract than women in the lowest lutein intake quintile (0.28 g/d). The trend was in the same direction in men, but did not reach significance. In a prospective study of women (Hankinson *et al.*, 1992) it was reported that among specific food items spinach, a lutein rich food, was most consistently associated with a lower relative risk. In a sub-study of the Nutritional Factors in Eye Disease Study of Beaver Dam, levels of individual carotenoids in serum were determined in 400 subjects 50 to 84 years. High levels of lutein in serum were significantly related to lower odds for nuclear sclerosis only in men who

smoked. In a cross-sectional study investigating the relationship between plasma concentrations of antioxidant vitamins and carotenoids and nuclear, cortical, and posterior subcapsular cataracts in a group of men and women ($n = 372$, 66–75 years), risk of posterior subcapsular cataract was lowest in those with higher concentrations of lutein (OR, 0.5; 95% CI, 0.2–1.0, P for trend = 0.012). High plasma concentrations of zeaxanthin were not associated with decreased risk (Gale *et al.*, 2001).

Omega-3 fatty acids

Cataract formation is associated with perturbations of lens membrane composition, structure and function (Borchman *et al.*, 1996; Kistler and Bullivant, 1989; Simonelli *et al.*, 1996) as well as changes in fatty acid composition (Rosenfeld and Spector, 1982). Studies in rats find that high intake of polyunsaturated fatty acids delays the cataract formation (Hatcher and Andrews, 1970; Hutton *et al.*, 1976). In a prospective study examining the relationship between dietary fat and cataract extraction in women ($n = 71{,}083$, 16-year follow-up), women in the highest quintile of long chain omega-3 fatty acids (0.21% of energy) had a 12% lower risk of cataract extraction compared to those in the lowest quintile (0.03% of energy) (Lu *et al.*, 2005) (relative risk = 0.88, 95% CI: 0.79–0.98, P for trend = 0.02).

16.3.2 Age-related macular degeneration (AMD)

Vitamin C

In the Eye Disease Case-Control Study (Seddon *et al.*, 1994) (356 cases, 520 controls) it was observed that persons in the highest and lowest intake quintiles (1039 and 65 mg/d, respectively) for vitamin C had the same prevalence of advanced AMD. In the Blue Mountains Eye Study, a population-based cohort study, it was found that compared with the lowest quintile, increasing baseline intakes of vitamin C, from diet and supplements, was associated with an increased risk of incidence of early age-related maculopathy (Flood *et al.*, 2002). In a recent population-based study out of the Nethelands, Van Leeuven *et al.* (2005) reported that an above-median intake of vitamin C, vitamin E, β-carotene and zinc compared with a below-median intake of at least one of these nutrients, was associated with a 35% reduced risk of AMD (hazard ratio, 0.65; 95% CI, 0.83–0.98). In persons with a below-median intake of all four nutrients, the risk of AMD was increased but not significantly (HR, 1.20; 95% CI, 0.92–1.56). However, West *et al.* (1994) reported that individuals with plasma vitamin C concentrations >80 μmol/L had a 45% lower prevalence of AMD compared with individuals who had concentrations <60 μmol/L. The Eye Disease Case-Control Study Group reported that individuals with serum vitamin C concentrations $\geq$91 μmol/L had a 30% lower prevalence of AMD compared with those who had concentrations < 40 μmol/L (EDCCSG, 1993). Evaluation of serum concentrations in patients with and with out age-related maculopathy found that levels of vitamin C were lower in late ARM ($n = 29$) than in early ARM ($n = 19$)

($p < 0.05$) but the two forms were not different that the controls (Simonelli *et al.*, 2002).

Vitamin E

Associations between plasma vitamin E concentrations and risk of AMD are inconsistent. The one study that has evaluated the role of dietary vitamin E and AMD risk reported no difference in prevalence of advanced AMD between individuals in the highest and lowest vitamin E intake quintiles (Seddon *et al.*, 1994). A protective effect of increased plasma vitamin E against AMD has been found in some studies (West *et al.*, 1994; EDCCSG, 1993), but not in others (Mares-Perlman *et al.*, 1995c; Sanders *et al.*, 1993). Evaluation of serum concentrations in patients with and with out age-related maculopathy found that levels of vitamin C were lower in late ARM ($n = 29$) than in early ARM ($n = 19$) ($p < 0.05$) but the two forms were not different that the controls (Simonelli *et al.*, 2002).

Lutein and zeaxanthin

The Carotenoids in Age-Related Eye Disease Study (CAREDS) used a cohort of 1787 women aged, between 50 and 79 years (Moeller *et al.*, 2006). There was no overall difference in the risk of AMD for the overall sample population. However, it was reported that women under 75 years with a high and stable intake of lutein and zeaxanthin (2.9 mg/d) had a 43% lower risk of intermediate stage AMD, compared to under those under 75 years of age with low lutein and zeaxanthin intake (0.8 mg/d). High and stable lutein and zeaxanthin intake was associated with a 74% lower risk of late-stage AMD, compared to low lutein and zeaxanthin intake. Women over 75 years with high intakes of lutein and zeaxanthin did not have reduced risks of AMD, compared to the lower intake group of the same age.

Results of a multicenter case-control study suggest that high intakes of carotenoid, particularly lutein and zeaxanthin, are related to lower risk of advanced neovascular AMD (Seddon *et al.*, 1994). This is similar to earlier findings from the First Health and Nutrition Examination Survey, in which low intakes of fruits and vegetables providing vitamin A were related to higher rates of all types of advanced AMD (Goldberg *et al.*, 1998). The Eye Disease Case-Control Study (1993) found after adjusting for other risk factors, people in the highest quintile of carotenoid intake had a 43% lower risk for neovascular AMD compared to those in the lowest quintile. Among the specific carotenoids, lutein and zeaxanthin were most strongly correlated with a reduced risk for age-related macular degeneration. In contrast, a nested case-control study as part of the Beaver Dam Eye Study, found no association with serum levels of lutein and zeaxanthin in 167 cases of early age-related macular degeneration and age-, sex-, and smoking-matched controls (Mares-Perlman *et al.*, 1995c). In a case-control study involving 72 cases and 66 control patients, the prevalence rate of AMD in patients with low lutein intake was about twice as high as that in patients with high intake (OR:2.4, 95% CI (1.1–5.1)) (Snellen *et al.*, 2002). Evaluation of

intake data into quartiles of lutein/zeaxanthin intake showed a clear dose-response relationship.

Omega-3 fatty acids

It has been suggested that atherosclerosis of the blood vessels that supply the retina contributes to the risk of AMD, analogous to the mechanism underlying coronary heart disease (Sarks and Sarks, 1994). Long chain omega-3 fatty acids may have a special role in the function of the retina in addition to their antithrombotic and hypolipidemic effects on the cardiovascular system. Docosahexaenoic acid (DHA) is the omega-3 fatty acid of key interest. DHA is a major fatty acid found in the retina (Fliesler and Anderson, 1983). Rod outer segments of vertebrate retina have a high DHA content (Fliesler and Anderson, 1983; Bazan *et al.*, 1986). Since photoreceptor outer segments are constantly being renewed, a constant supply of DHA may be required for proper retinal function and a marginal depletion may impair retinal function and influence the development of AMD.

Epidemiologic studies examining the relationship of DHA or fish intake with AMD suggest a trend towards a protective relationship. In a prospective follow-up study of the Nurses' Health Study and the Health Professionals Follow-up Study, men and women ($n = 72{,}489$) with no diagnosis of AMD were followed for 10–12 years. Odds of AMD decreased with increased DHA intake (top versus bottom quintile of RR: 0.70; 95% CI: 0.52-0.93; P for trend = 0.05). However, the relationship of DHA did not remain (OR for highest vs. lowest of DHA intake = 0.8; 95% CI, 0.5–1.1) when modeled simultaneously with intake of other dietary lipids. These investigators also examined the association of fish intake (a major source of DHA) with AMD risk. Consumption of >4 servings of fish/wk was associated with a 35% lower risk of AMD compared with $\leq$3 servings/mo (RR: 0.65; 95% CI: 0.46–0.91; P for trend = 0.0009) in pooled multivariate analysis (Cho *et al.*, 2001a). Of the individual fish types examined, a significant inverse association was found only with tuna intake. The pooled RR of participants who ate canned tuna more than once per week compared with those who consumed it less than once per month was 0.61 (95% CI: 0.45–0.83).

The Dietary Ancillary Study of the Eye Disease Case Control Study (1993) reported results for 349 participants with neovascular AMD and 504 control subjects without AMD (Seddon *et al.*, 2001). In demographically adjusted analyses, increasing intake of linoleic acid was significantly associated with higher prevalence of AMD (P for trend = 0.004). This association remained in multivariate analyses, with an OR for the fifth versus first quintile of 2.00 (95% CI, 1.19–3.37) (P for trend = 0.02). In contrast, intake of omega-3 fatty acids showed an inverse relationship with AMD in demographically adjusted analyses (P for trend = 0.01) but became non significant after controlling for confounding variables, e.g. cigarette smoking. When the study population was stratified by linoleic acid intake ($\leq$5.5 g/d or $\geq$5.6 g/d), the risk for AMD was significantly reduced with high intake of omega-3 fatty acids among those with low linoleic acid intake (P for trend = 0.05; P for continuous variable = 0.03). In contrast,

among individuals with high linoleic acid intake, no significant association was seen for omega-3 fatty acid intake after controlling for other confounding variables. The authors commented that these findings suggest a competition between n-3 and n-6 fatty acids and that both the level of n-3 fatty acids and its ratio to the n-6 acids are important. These results are similar to a more recent report involving a prospective cohort study of 261 persons aged 60 years or older at baseline with an average follow-up of 4.6 years. In this study, 101 patients with AMD progressed to advanced AMD. It was reported that higher fish intake (>2 servings/week versus <1 serving/week) was associated with a lower risk of progression to advanced AMD among subjects with lower linoleic acid intake (OR 0.36; 95% CI, 0.14–0.95) (Seddon *et al.*, 2003).

A relationship between fish intake and late ARM (neovascular AMD) or geographic atrophy was not measured in the Beaver Dam Eye Study, a retrospective population-based study. However, fish intakes were low (Mares-Perlman *et al.*, 1995d) and it is possible that the intake of omega-3 fatty acids in this population was not varied enough to detect a difference in risk for AMD.

Heuberger *et al.* (2001) evaluated the associations between fish intake and age-related maculopathy (ARM) in the Third National Health and Nutrition Examination Survey. Persons aged 40 to 79 years ($n = 7405$) were included in analyses for early ARM ($n = 644$); those 60 years or older ($n = 4294$) were included in analyses for late ARM ($n = 53$). Consuming fish more than once a week compared with once a month or less was associated with ORs of 1.0 for early ARM (95% CI, 0.7–1.4) and 0.4 for late ARM (95% CI, 0.2–1.2) after adjusting for age and race. Adjusting for other possible risk factors did not influence these relationships (Heuberger *et al.*, 2001). These investigators concluded that no associations were observed between fish intake and ARM in this population. However, associations with late ARM, while not statistically significant, the ORs were consistent with observations of inverse association reported by others (Cho *et al.*, 2001a; Smith *et al.*, 2000).

The Blue Mountains Eye Study (BMES) was a population-based survey of vision, common eye diseases and diet in an urban population of 3654 people aged 49 years and older (Smith *et al.*, 2000). In the 2915 subjects evaluated for fish intake, there were 240 cases of early ARM and 72 cases of late ARM identified. In this study, more frequent consumption of fish appeared to protect against late ARM, after adjusting for age, sex and smoking. The protective effect of fish intake commenced at a relatively low frequency of consumption (1–3 times per month compared with intake <1 time per month; OR: 0.23; 95% CI: 0.08–0.63). The ratio of cases to controls in these intake groups was 6/777 and 17/380, respectively. The OR for intake >5 times/week compared with <1 time per month was 0.46 (95% CI: 0.12–1.68). The authors suggested that there may be a threshold protective effect at low levels of fish intake, with no increased protection form ARM at increased fish intake. In this study, there was little evidence of protection against early ARM.

Zinc

The zinc concentration in the retina is one of the highest levels in the body, suggesting a special importance to the eye (Newsome *et al.*, 1992). In fact, in a study by Newsome *et al.* (1988), zinc supplementation given to elderly people with early stages of AMD resulted in better maintenance of visual acuity than in those receiving placebo. However, in a prospective study of zinc intake and risk of AMD, in which 66,572 women and 37,636 men ($\geq$ 50 years) were followed for 10 years it was found that after multivariate adjustment for potential risk factors, the pooled relative risk was 1.13 (0.82–1.56) among participants in the highest quintile of total zinc intake (25.5 mg/d for women, 40.1 mg/d for men) compared with those in the lowest quintile (8.5 mg/d for women, 9.9 mg/d for men) (Cho *et al.*, 2001b). The relative risk of highest compared with lowest quintile was 1.04 (95% CI, 0.59–1.83) for zinc intake from food. Subjects who took zinc supplements had a pooled multivariate relative risk of 1.04 (95% CI, 0.75–1.45). It was concluded from this large prospective study that zinc intake either in food or supplements was not associated with a reduced risk of AMD.

16.4 The effect of nutrient supplements on eye disease risk

Supplemental vitamins C and E have been long available to the general public. Currently, there are a variety of supplement products available in health food stores that contain lutein in amounts of 6–25 mg/capsule. At this point, lutein is found in only one multivitamin product in much smaller amounts (0.25 mg/capsule).

16.4.1 Cataract

Jacques *et al.* (1997) observed a >75% lower prevalence of early opacities in women who used vitamin C supplement for $\geq$ 10 yrs. None of the 26 women who used vitamin C supplements for $\geq$ 10 yrs had more advanced nuclear cataract. Hankinson *et al.* (1992) observed that women who reported use of vitamin C supplement for $\geq$10 yrs had a 45% reduction in rate of cataract surgery. The study of Robertson *et al.* (1989) observed that the prevalence of cataract in persons who consumed vitamin C supplement of >300 mg/d was approximately one-third the prevalence in persons who did not consume vitamin C supplements. However, Chasen-Taber *et al.* (1999b) prospectively examine the association between vitamin supplement intake and the incidence of cataract extraction during 12 years of follow-up in a cohort of 73,956 female nurses. After adjusting for cataract risk factors, including cigarette smoking, body mass index, and diabetes mellitus, there was no difference in the incidence of cataract between users of vitamin C supplements for 10 years or more and non users.

Nadalin *et al.* (1999) cross sectionally examined the association between prior supplementation with vitamin E and early cataract changes in volunteers. Of 1,111 participants 26% reported prior supplementation with vitamin E. Only

8.8% of these participants took supplementation greater than the recommended daily intake (10 mg/d). A statistically significant association was found between prior supplementation and the absence of cortical opacity, after adjusting for age. However, the levels of nuclear opacity were not statistically different between those who reported intake and those with no prior vitamin E supplementation. Leske *et al.* (1998) examined the association of antioxidant nutrients and risk of nuclear opacification in a longitudinal study. The risk of nuclear opacification at follow-up was decreased in regular users of multivitamin supplements, vitamin E supplements, and in persons with higher plasma levels of vitamin E. The investigators concluded that in regular users of multivitamin supplements, the risk of nuclear opacification was reduced by one third. They also reported that in regular users of vitamin E supplement and persons with higher plasma levels of vitamin E, the risk was reduced by approximately half. These results are confirmed by Robertson *et al.* (1989) who reported that the prevalence of cataract was 56% lower in persons who consumed vitamin E supplement than in persons not consuming supplements. One study observed no relation between risk of cataract and vitamin E supplements (Hankinson *et al.*, 1992).

To date, there are few data from intervention trials of vitamins and cataract risk. In a recent study, it was reported that a high dose combination of antioxidants (vitamins C and E, beta-carotene, and zinc) had no significant effect n the development or progression of cataract (AREDSRG, 2001). The LINXIAN trial (Sperduto *et al.*, 1993) examined the role of antioxidants in prevention of cataract, and the effect is not clear. The intervention was a combination dose of 14 vitamins and 12 minerals. Therefore, a specific role of any one nutrient could not be accurately evaluated. The multivitamin component demonstrated that nutrition can modify the risk of nuclear cataract, but specific nutrients were not evaluated. Also, the population examined had suboptimal nutritional intakes at the study start and the effect may have been due to a correction of certain nutrient deficiencies. The Alpha-Tocopherol Beta-Carotene, a population-based, controlled clinical trial to prevent lung cancer evaluated the effect of nutritional antioxidants on the incidence of age-related cataract extraction (Teikari *et al.*, 1998b). Subjects were randomly assigned to one of four regimens (α-tocopherol, 50 mg/d; β-carotene, 20 mg/d; both, or placebo). Follow-up was for 5–8 years. These investigators reported that supplementation with these antioxidants does not affect the incidence of cataract extractions among male smokers.

The Roche European-American Anticataract Trial (REACT) was carried out to examine if a mixture of oral antioxidant micronutrients (β-carotene, 18 mg/d; vitamin C, 750 mg/d; vitamin E, 600 mg/d) would modify the progression of age-related cataract (Chylack *et al.*, 2002). This was a multi-center prospective double masked randomized placebo-controlled 3-yr trial in 445 patients with early age-related cataract. REACT demonstrated a statistically significant positive treatment effect after two years for US patients and for both subgroups (US, UK) after three years, but no effect for the UK patients alone. The conclusion from this study was

that daily supplementation with these nutrients for three years produced a small deceleration in progression of age-related cataract.

16.4.2 Age-related macular degeneration (AMD)

The Age-Related Eye Disease Study (AREDS) reported that high level of antioxidants and zinc significantly reduce the risk of AMD and its associated vision loss (AREDSRG, 2002). It was found that people at high risk for developing advanced stages of AMD (people with intermediate AMD or advanced AMD in one eye but not the other eye) lowered their risk by about 25% when treated with a high-dose combination of vitamins C and E, beta-carotene, and zinc. In the same high risk group the nutrients reduced the risk of vision loss caused by advance AMD by about 19 percent. For those subjects who had either no AMD or early AMD, the nutrients did not provide a measured benefit. Because single nutrients were not evaluated, specific effects could not be determined.

It has been reported that the prevalence of AMD in persons who consumed vitamin C supplement for > 2 yrs was similar to those who never took vitamin C supplements (Kistler and Bullivant, 1989). In a study conducted by Seddon *et al.* (1994) the prevalence of AMD was also similar between those who took vitamin E supplement for > 2 yrs and those who never took vitamin E supplements. The Alpha-Tocopherol Beta-Carotene Trial, a population-based, controlled clinical trial to prevent lung cancer valuated the effect of nutritional antioxidants on AMD (Teikari *et al.*, 1998a). Over 29,000 smoking men aged 50–69 years were randomly assigned to α-tocopherol (50 mg/d), β-carotene (20 mg/d), both or placebo. There were 728 people randomized to any antioxidant and 213 to placebo. The results of this study found no beneficial effect of long-term supplementation with α-tocopherol and/or β-carotene on the occurrence of age-related maculopathy among smoking males. Although this was a large, high quality study there were only 14 cases of late AMD. Thus, limiting the ability to assess the effect of antioxidant supplementation on AMD prevention.

AREDS I reported that high level of antioxidants vitamin C, 500 mg; vitamin E, 400 IU; β-carotene, 15 mg; zinc, 80 mg) taken daily for seven years, significantly reduce the risk of AMD and its associated vision loss (AREDSRG, 2001). The study involved 4757 participants, 55–80 years of age in 11 clinical centers in the US. It was found that people at high risk for developing advanced stages of AMD (people with intermediate AMD or advanced AMD in one eye but not the other eye) lowered their risk by about 25% when treated with a high-dose combination of vitamins C and E, beta-carotene, and zinc. In the same high risk group the nutrients reduced the risk of vision loss caused by advance AMD by about 19%. For those subjects who had either no AMD or early AMD, the nutrients did not provide a measured benefit. Because single nutrients were not evaluated, specific effects could not be determined.

Lutein and zeaxanthin supplements have only recently become available to the general public. Therefore, time has not allowed for the adequate study of the

effect of these nutrient supplements of the prevalence of either cataract or AMD. The effects of supplementation with these food components will be addressed in AREDS II.

Age-Related Eye Disease Study II (AREDS II) began in early 2006 (www.nei.nih.gov/neitrials/viewStudWeb.aspx?id=120). This study aims to refine the findings of AREDS which demonstrated that oral supplementation with high-dose antioxidant vitamin and mineral (vitamins C and E, β-carotene, zinc, and copper) reduced the risk of advanced AMD by 25% (AREDSRG, 2001). AREDS II aims to improve on this by evaluating the role of n-3 fatty acids as well as the carotenoids, lutein and zeaxanthin.

16.5 Clinical recommendations/treatment guidelines

The inconsistencies among studies in terms of the amount of nutrient required for protection against eye disease makes it difficult to make specific recommendations for dietary intakes of these nutrients. Therefore, it may be more practical to recommend specific food choices rich in vitamins C and E, lutein, zeaxanthin, omega-3 fatty acids and zinc. This will allow for benefit from possible effects of the components in food that may also be important. This necessitates an awareness of dietary sources of nutritional antioxidants. Good sources of vitamin C include citrus fruit, berries, tomatoes, and broccoli (USDA, 2006). Good sources of vitamin E are vegetable oils, wheat germ, whole grain cereals, nuts, and legumes (USDA, 2006). The two foods that were found to have the highest amount of lutein and zeaxanthin are kale and spinach. Other major sources include broccoli, peas, and brussel sprouts (Mangels *et al.*, 1993).

A healthy diet including a variety of fresh fruit and vegetables, legumes and nuts, will have many benefits, will not do any harm, and will be a good source of the antioxidant vitamins and minerals implicated (but not proven) in the etiology of cataract and AMD. There is no evidence that nutrient-dense diets high in these foods, which provide known and unknown antioxidant components, are harmful. In fact, intake of fruits and vegetables is associated with reduced risk of death due to cancer, cardiovascular disease, and other causes. Thus, recommendations such as consuming a more nutrient-dense diet, i.e. lower in sweets and fats, and increasing levels of fruit and vegetable intake do not appear to be harmful and may have other benefits despite their unproven efficacy in prevention or slowing disease. Until the efficacy and safety of taking supplements containing nutrients can be determined, current dietary recommendations (USDA, 2005) are advised.

16.6 Conclusions

The hypothesis that certain nutrients may protect against the cataract and AMD is a plausable one given the role of oxidative damage in the etiology of these diseases and their high concentrations in ocular tissue. However, the studies

examining nutrient and eye disease relationships are not entirely consistent. In part, this may be due to methological differences among the various studies. Also, there are limitations to such studies that examine relationships between a nutrient and disease because calculations from dietary recall may not always accurately estimate nutrient intakes due to limitations of the database or recall abilities of the subjects. Furthermore, a single blood value for a nutrient may not always be an accurate indicator of long-term status. In addition, the high degree of correlation in intake among the various dietary micronutrients makes it difficult to determine which specific nutrient or nutrients are related to the observed relationships. Despite these drawbacks, a possible protective role of vitamins C and E and the carotenoids lutein and zeaxanthin cannot be dismissed given the number of studies that found a protective effect and the very few studies that found a negative effect. In some cases, it may be difficult to measure an outcome if nutrient intake levels are at those found in diet alone. That is, dietary and plasma levels may not be sufficiently high to see an effect. In this regard, review of studies that have examine the relationship between supplemental nutrient intake with cataract and AMD risk may be useful. Although data regarding the use of nutrient supplements suggests protection in cataract and AMD. The research to date has not sufficiently evaluated the effectiveness vs. safety of nutrient supplements. But advocating the use of nutrient supplementation must be done with a cautionary note given that there have been trials which have suggested that supplementation with beta-carotene may have an adverse effect on the incidence of lung cancer in smokers and workers exposed to asbestos (Omenn et al., 1996; ATBCCPSG, 1994). Clearly further trial, such as the upcoming AREDS II trial, are warranted to address the usefulness nutrient supplementation in eye disease prevention.

It is likely that cataract and AMD develops over many years and the cause of these diseases is due to many factors. There are likely to be differences in the potential protective effect of certain nutrients depending on the stage of the disease.

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17

Beauty food: nutrition to support the skin

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Abstract: The following chapter gives an overview on how nutrition can influence the skin. The first part of the chapter gives background information on the skin, its functions and the skin ageing process. In the second part, nutrients and their possible effects on skin are presented. This is followed by examples on how to incorporate these nutrients into food formulations, taking both food regulations and technological challenges into account. In the last part, an outlook for possible future trends with regard to consumer expectations as well as technologies is given.

Key words: anti-ageing, antioxidants, skin, fatty acids, carotenoids.

17.1 Introduction

Beauty is directly linked to a clear and smooth skin and is seen as a synonym for health, vitality, mental fitness and physical attractiveness. The need to fulfil these social requirements is reflected in the growing beauty food market and the increasing number of new product developments in the area of beauty foods and food supplements with skin-related beauty claims. A recent market study (Datamonitor, 2006) demonstrates that consumers are supplementing diets to maintain and enhance their looks. Desired effects include reducing of wrinkles or strengthening and beautifying of hair. The global oral beauty supplement market is said to triple from 2000 to 2010 in Europe as well as in the US. The most important consumer group are females 35–65 years old (Datamonitor, 2006). Foods can affect how we feel and how we look. A sufficient and balanced intake of nutrients from our diet can affect our health and overall body

condition, which might be visible through our skin, hair and nail appearance as such (Miller, 1989). Healthy diets may help to protect against undesired skin conditions, such as dry skin and may help to slow down the skin ageing process.

The following chapter focusses on the relation between nutrition and skin. The chapter starts with background information about skin structure and functions, including effects of the antioxidant network in protection against UV-light-induced damage, as well as an overview of the skin ageing process. In the second part, nutrients, such as fatty acids, vitamin E, carotenoids and selected food grade plant extracts and their possible effects on skin are presented. This is followed by some guidelines on how to apply these nutrients into food formulation, taking into account food regulations as well as technological challenges. In the last part, an outlook for possible future trends with regards to consumer expectations as well as technologies is given.

17.2 Skin

All living organisms have skin-like structures which build the interface between the internal (body) and external (environment) worlds. Because of environmental factors, in particular temperature, sun and humidity, and the large surface area of the skin, it is exquisitely designed to perform a variety of protective and life-sustaining functions. This is achieved by the specific architecture of the skin and its derivatives (hair, sweat glands, etc.).

17.2.1 Skin structure

The skin is one of the largest organs of the body. With a surface area of approximately 1.8 m^2, the skin accounts for an estimated 15% of our body mass. The skin structure varies depending on which part of the body it covers; therefore it is difficult to define 'normal' skin. The epidermis is approximately 1 mm thick although the thickness can considerably vary depending on body location (eyelids: 0.05 mm; palms and soles: 1.5 mm). Typical variations, as known by most people, are that the scalp and genital areas generally have more hair than the abdomen or inner arms and that the face tends to be more greasy than the shins. Nevertheless, the skin has certain structural properties common to all areas. The skin can be divided into three main compartments: the epidermis, the dermis and the hypodermis (i.e., the adipose tissues and muscles). However, the latter is not always considered to be part of the skin, and therefore we will not discuss the hypodermis in this paper.

Epidermis

The epidermis is the outer layer of the skin and in certain parts it is specialized to form the skin appendages such as hair and nails. The main cell type is the keratinocyte which produces keratins – important fibrous proteins that provide

structural integrity and which are also found in nails and hair. Other cell types are:

- melanocytes which produce the melanin pigments responsible for skin color and ultraviolet light (UV)-protection (tanning);
- the Langerhans cells, important antigen presenting cells, which function as sentinel cells for the immune system; and
- the Merkel cells and free nerve endings, responsible for some sensorial properties, e.g. touch, heat and cold.

The epidermis is an avascular stratified epithelium with a rapidly proliferating basal layer which exhibits progressive differentiation. The inner layer, the stratum germinativum, produces the basal cells which proliferate, wander upwards, thereby changing their shape and function until they reach the outer layer, the stratum corneum. The terminally differentiated keratinocytes of the stratum corneum are often termed corneocytes. They are compact protein-rich lipid-depleted dead cells of polyhedral shape and are surrounded by the lamellar lipid layers typical of the S. corneum.

The ability of the skin, to maintain its water content and that of our body is associated with the organization of the stratum corneum. The latter plays a predominant role in maintaining the skin barrier function. During the differentiation process, the cytoplasm is filled with keratohyalin granules, keratin tonofibrils and fillagrin. The water content is greatly reduced from approximately 70% (basal layer) to 15% (S. corneum). In addition, during the differentiation process, lamellar lipids, composed of ceramides, phospholipids, cholesterol, glucosylceramides, triglycerides and free fatty acids, are secreted into the intercellular spaces. These changes lead to the formation of a 'hydrophobic' environment which facilitates the protective functions of this layer in keeping the body from drying out and reducing the possibilities for cutaneous uptake of substances and for microbial attack. Because the corneocytes with their extracellular matrix give the impression of having a wall-like structure, the stratum corneum is often described with the help of a brick (corneocytes) and mortar (extracellular lipids) model. As the epidermis and stratum corneum are constantly being renewed, the corneocytes undergo proteolytic degradation of the desmosomes, the structures joining the cells, and are continuously sloughed off (desquamation). The additional function of this renewal process is eliminating damaged cells and toxins.

Dermis

The dermis (corium) is a highly vascularized and innervated connective tissue layer that lies between the epidermis and the hypodermis. Depending on its location, the thickness ranges form 0.6 mm (eyelids) to 3 mm (palms). It provides the skin with tensile strength and elasticity. It houses the hair follicles that are lined with epidermal tissues, as well as the sweat and sebaceous glands. Various mechanoreceptors reside in this layer that detects pressure, vibration, touch and temperature. The main cell type is the fibroblast which produces the

intricate network of the extracellular matrix containing elastins, collagens, proteoglycans and glucosaminoglycans. The dermis is made up of two distinct regions, the uppermost papillary dermis and the lower reticular region. The papillary dermis contains the dermal portion of the dermal epidermal junction (DEJ). The DEJ is characterized by conical structures of collagen-rich dermal cells, the dermal papillae, which extend into the epidermis whereby the cells of the stratum germinativum are linked into these structures forming a downward thickening of the epidermis (so-called the rete pegs). The cells of DEJ collaborate during the morphogenesis of the skin appendages and in wound-healing and give the skin mechanical support. The papillary dermis is also highly vascularized with capillaries extending up into the dermal papillae, thus helping to nourish the epidermal cells. It contains small diameter collagen bundles and oxytalan elastic fibers. The reticular dermis forms the bulk of the dermis and is characterized by a dense meshwork of large diameter collagen bundles and band like branching elastin fibers.

Collagens (over 20 different collagens are known) are the main constituents of the dermis and account for approx. 75% of the skin's dry weight. In the dermis, the fibrillar collagen types I, III, and IV are the most prevalent. Collagen type VII found at the DEJ forms anchoring structures with the interstitial collagens of the dermis. Most collagens are oriented parallel to the body and are interconnected with elastins and proteoglycans. The turnover of the extracellular matrix is tightly regulated by metalloproteinases (MMPs), which in general degrade collagen, and their counterparts, the tissue inhibitors of metalloproteinases (TIMPs). Approximately 20 MMPs and 4 TIMPs are known. The interstitial collagenase MMP-1 is the best characterized and catalyzes the initial steps in the degradation of fibrillar collagen types I and III. TIMP-1 preferentially inhibits MMP-1. In skin, particularly upregulation of collagenase-1 (MMP-1), stromelysin-1 (MMP-3) and gelatinase A (MMP-2) expression and downregulation of TIMP-1 are involved in the lysis of dermal collagen and elastin fibers typical of skin ageing (Hornebeck, 2003).

17.2.2 Functions of the skin

The primary role of the skin is to provide a barrier which protects against potentially damaging environmental influences and physical trauma. Various cells located within the skin, e.g. Langerhans cells, play a pivotal role in immune responses. The stratum corneum constitutes our skin barrier and provides further protection against external insults, e.g. by very effectively impeding the penetration of many irritants and toxic agents, gives protection against UV irradiation and keeps us from drying out by controlling evaporation of water from our bodies. It not only serves as a protective barrier but via constriction or dilatation of the cutaneous blood vessels, sweating, etc., it has significant functions in thermoregulation. It is of utmost importance in receiving sensorial stimuli and in 'communication' processes. The skin produces various substances, such as antimicrobial peptides and Vitamin D precursors that are also important for the

overall health of the skin and body. As the antioxidant network and UV-induced processes play a major role in the ageing of the skin, these two aspects will be discussed in the following.

The antioxidant network of the skin

As the interface between the body and the environment, the skin is continuously exposed to environmental and metabolic insults. The skin is rich in lipids, proteins and DNA – all biological targets for oxidative damage – making it quite susceptible to oxidation processes. Typical damage incurred is DNA damage, oxidation or alkylation of lipids and proteins and peroxidation of lipid membranes. The delicate balance between antioxidants and pro-oxidants can be tipped in favor of the pro-oxidants by events that induce oxidative stress, such as an excess of reactive oxygen species (ROS). ROS can be induced by the exposure to solar UV-irradiation, pollution or metabolic disturbances, etc., which in turn can lead to a depletion of antioxidants in the skin. ROS are a major contributor to skin damage resulting in skin ageing, skin disorders and skin diseases. The skin is equipped to give both physical and chemical protection against these insults and therefore possesses an intricate network of antioxidant and enzyme systems to counteract the damage incurred by them (Thiele and Elsner, 2000). All cells of the body contain antioxidant networks in which several antioxidative systems interact and replenish themselves. The epidermis is particularly well equipped with antioxidant defenses. The major antioxidants found in the epidermis are lipid-soluble antioxidants such as vitamin E and the carotenoids, the water-soluble antioxidants, vitamin C, glutathione (GSH) and uric acid, as well as the enzymes superoxide dismutase (SOD), catalase, glutathione reductase and glutathione peroxidase (GPX). A schematic representation of the main antioxidants of the skin and their 'recycling pathways' is shown in Fig. 17.1.

UV and the skin

Exposure to small amounts of ultraviolet light (UV; UVB: 290–320 nm; UVA: 320–400 nm) has a beneficial role in human health. For instance, Vitamin D3 (cholecalciferol) is produced in the skin when light energy is absorbed by the precursor molecule 7-dehydrocholesterol. Among its other physiological roles, vitamin D plays a major role in mineral homeostasis by facilitating intestinal absorption of calcium, phosphorus and other minerals. It thereby is involved in regulating bone growth and turnover, and deficiencies can lead to osteoporosis, rachitis and other skeletal problems. Whereas it is well recognized that excessive sun exposure leads to an increased incidence of skin cancer, recent epidemiological studies have revealed an inverse association between sun exposure and the incidence of certain cancer types, e.g. non-Hodgkin lymphoma, colon or breast cancer. This is in part attributed to the beneficial effects Vitamin D which is produced by the skin during UV-exposure (Lucas *et al.*, 2006; Kricker and Armstrong, 2006). Lack of sufficient exposure to sunlight and reduced production of Vitamin D3 by the ageing skin, requires dietary supplementation

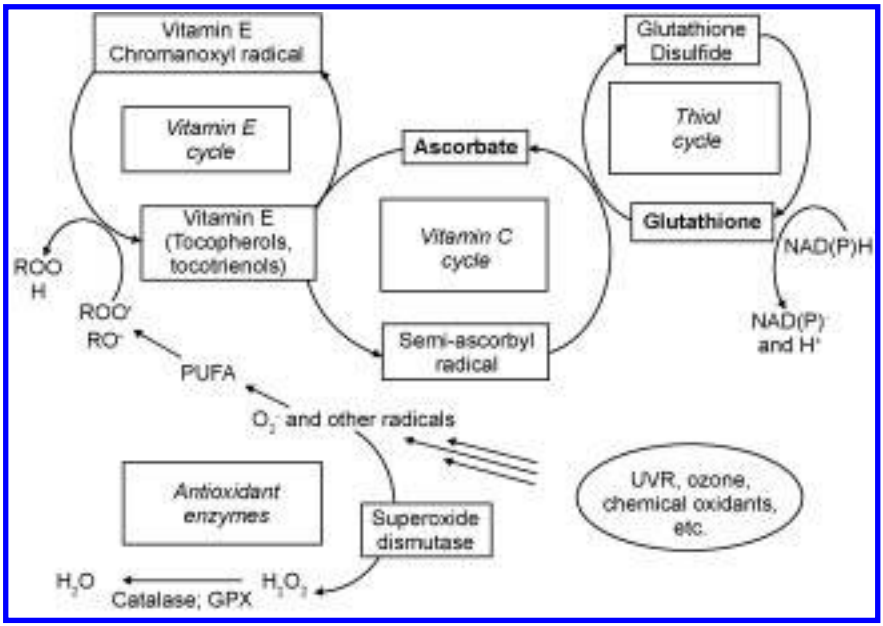

Fig. 17.1 Schematic representation of the antioxidant network of the skin and the recycling pathways (adapted from Thiele *et al.*, 2001).

to avoid deficiencies. This can in part be achieved via nutritional pathways. Although UV light is a fundamental necessity for life, it can also have hazardous effects on the skin. The mechanisms underlying UV radiation's influence on health are not restricted to its instrumental role in the development of skin cancer, in particular malignant melanoma, but also in the profound effects it has on local and systemic inflammatory responses. Exposure to UVB irradiation can significantly suppress the immune system by inhibiting the protective cell-mediated immunity and also contributes to the initiation as well as development and perpetuation of several skin disorders, e.g. exacerbation of infectious diseases (Herpes simplex), induction of skin cancer as well as of photosensitive diseases such as solar urticaria. Whereas UVB generally only penetrates to the epidermis, UVA irradiation can reach the dermis. The effects of UVA accelerate skin ageing by causing cross linking of elastic fibers and qualitative alterations in collagen structure thus leading to the loss of tensile strength and wrinkle formation.

Our skin has developed systems to counteract some of the deleterious effects of UV. For instance, skin is pigmented by melanin, the substance that also gives us our suntan, which acts as a natural sunscreen. The DNA damage caused by UVB is considered to be a central etiological factor for the development of malignant melanoma and other skin cancers. DNA damage is incurred to DNA both directly via UV-absorption and formation of pyrimidine dimers and indirectly via damage induced by ROS. The use of antioxidants to counteract these effects, e.g. supplementation with vitamin E and vitamin C over a period

of three months resulted in a reduction in the generation of thymine-dimers (cyclobutane pyrimidine dimers) and pyrimidine-pyrimidone (6-4) photo-products, typical damage done to DNA by UVB-irradiation (Placzek *et al.*, 2005). Because glutathione (GSH) plays a central part in the endogenous defense against UV radiation, an increase in GSH might provide photo-protection. One study (Steenvoorden *et al.*, 1998) showed that the protection against UV-induced reactive intermediates depends on a general antioxidant action of these thiols, rather than only on their role as GSH precursors.

17.2.3 Skin ageing

Ageing has been defined as the accumulation of molecular modifications and damage which ultimately manifest themselves as macroscopic clinical changes (Waller and Maibach, 2006). Skin ageing is probably the most obvious visual marker for chronological ageing. Considering the negative way the Western world regards senescence especially in regard to appearance, it has a profound effect on the psychological wellbeing of the individual. Skin ageing is a natural phenomenon based on a continuous and complex interplay between intrinsic (chronological; innate, programmed) and extrinsic (environmental, wear and tear) ageing. Skin ageing occurs in every individual and its progression is consequently influenced by a combination of several factors. These factors include the exposure to environmental insults (UV-irradiation, xenobiotics, etc.), genetics, illness, hormonal changes, metabolic processes and nutritional balance (Thomas, 2005). An ageing skin is characterized by wrinkles, loss of elasticity and thinning of the skin (skin atrophy; Contet-Audonneau *et al.*, 1999). Pigmentation disorders, such as age spots (lentigines), localized hypo- and hyper-pigmentation may give the skin a mottled appearance. As we age, the number of sweat glands often decreases and sebaceous gland activity is reduced (Zouboulis and Boschnakow, 2001). Therefore, many older people tend to suffer from dry skin (xerosis) and the decreased moisture content makes the skin dry and flaky. This is often accompanied by varying degrees of itchiness, which makes the skin more prone to irritation. Scratching leads to a disruption of the skin barrier so that infections and inflammation can occur. Thinning of the skin (in part due to the retraction of the rete pegs), weakening of connective tissue and a decrease in adipose tissue in the hypodermis makes the skin frail and increases its susceptibility to bruising. Epidemiologists have established that the dry skin typical in elderly individuals increases the propensity to develop pressure sores (decubitus ulcers) (Klingmann, 1999). Changes in the immunological status of the skin and the progressive accumulation of DNA damage over time increases the likelihood of cancer in ageing skin.

Morphological changes during ageing

A plethora of morphological and cellular changes accompany the ageing process of the skin. Within the epidermal layer, the stratum corneum thickens, the epidermis thins and the dermo-epidermal junction flattens. This decrease in area

between the dermal and epidermal compartments results in fewer anchoring type molecules (e.g., desmoplakins of the desmosomes, collagen IV and VII) being able to uphold skin stability. In addition, the reduction in available area also leads to a reduction of nutrient transfer between the dermis and epidermis. Desquamation and proliferation is impaired and keratinocyte differentiation is disturbed (Gilhar *et al.*, 2004). With age, restoration of the skin barrier after damage is impaired. There is also progressive loss of moisture in the skin, in part due to the decline in levels of the natural moisturizing factor (NMF) and the reduced production of sebum by the sebocytes. In addition, changes in sweating and sweat composition lead to dehydration of the skin. This in part leads to the loss of elasticity and turgor of the older skin. Melanocyte numbers decrease with ageing and their distribution becomes less uniform, which in turn leads to the formation of pigmental disturbances, e.g. lentigines (age-spots), freckles and areas of hypopigmentation. The dermis also atrophies. Symptoms are a reduction in collagen turnover, an increase in the disorder of collagen and elastin crosslinking and a decrease in the number of elastic fibers and in mucopolysaccharide content (e.g., hyaluronic acid). Glycosaminoglycans (GAGs; e.g. chondoitin sulfate) play a major role in maintaining hydration, but also decrease with ageing. The number of mast cells is reduced and, together with Langerhans cell and T cell dysfunction (Grewe, 2001; Aspinall, 2003), which accounts for some aspects of the immune compromised status of the skin in elderly people. The vasculature, in particular the number of vertical capillary loops is decreased thus leading to a decreased cutaneous blood flow (Ryan, 2004). The number of Pacinian (pressure) and Meissner (touch) corpuscules is diminished and the number of epidermal nerve fibers is reduced leading to alterations in the perception of sensation and tactile spatial acuity (Leveque *et al.*, 2000).

Photoageing

UV irradiation is probably the most important factor leading to skin ageing which is therefore also termed photoageing. UV irradiation leads to the formation of deep wrinkles, leather-like skin, elastosis, spider vens (telangiectasias) and pigmentation disorders. Changes in the epidermis caused by the sun include thinning of the epidermis and slight thickening of the stratum corneum. In the dermis, UV irradiation causes collagen to break down at a higher rate than during intrinsic ageing. It damages collagen fibers and causes the accumulation of abnormal nonfunctional elastin. Metalloproteinase (MMPs) are produced in larger quantities. TIMP (tissue inhibitors of metalloproteinase) expression is reduced which leads to further break-down of collagen. This explains the formation of the deep wrinkles in photo-damaged skin. Typical cellular manifestations of chronic exposure to UV-irradiation are DNA-damage, local and systemic immune suppression, accompanied by prominent alterations in the extracellular matrix of the dermis. The latter is not only characterized by the accumulation of disorganized elastin and structural destruction of dermal collagen fiber bundles. The unifying pathogenic agents are reactive oxygen species (ROS), particularly caused by UVA irradiation, which deplete the

Table 17.1 Overview of features of chronologically aged and photoaged skin

Feature	Chronological ageing (intrinsic ageing)	Photoageing (extrinsic ageing)
Clinical appearance	Smooth, unblemished, loss of elasticity	Nodular, leathery, blotched, wrinkling, often deep
Skin surface marking	Overall maintenance of geometric patterns	Markedly altered and often effaced
Viable epidermis	Thinner than normal; less proliferation	Acanthoic, later atrophied; higher proliferation
Dermis	• Decrease in dermal thickness • Collagen bundles appear denser due to decreased proteoglycans and hyaluronic acid • Increased elastogenesis, followed by elastolysis	• Thick, degraded non-functional elastic fibers • Fragmented collagen bundles • Increased collagenase activity • Increased elastogenesis followed by massive degeneration

antioxidant defence systems in the skin. ROS lead to the formation of DNA adducts, protein oxidation and lipid peroxidation as well as to signal transduction cascades leading to inflammatory processes and aberrant gene expression. An overview of varying features between chronologically aged and photoaged skin is given in Table 17.1.

17.3 Nutrients

The main skin-related 'beauty food' categories are sun protection, moisturizing (dry skin), skin tanning, impure skin and anti-cellulite. Reasons for an impure skin could be an unbalanced diet or hormonal dysbalance caused by stress due to amongst others a high workload and a lack of sleep. Indications to use such 'beauty foods' are very similar to those made for traditional cosmetic products.

The importance of optimal nutrient supply to the skin has been recognized for long, but largely focused on 'traditional' nutrients such as vitamins. These are important in all aspects of cell renewal, due to their central role in many aspects of cellular metabolism. So-called 'skin vitamins' include vitamin C, which acts as antioxidant and is involved in the synthesis of collagen, vitamin A, which is important for cell differentiation and the maintenance of all epithelia, as well as several members of B vitamins, particularly pantothenic acid, biotin and niacin. In addition, antioxidants, specific fatty acids and – most recently – various plant extracts have been investigated for their effects on skin. These are further discussed below.

17.3.1 Vitamin E

Vitamin E has long been an essential ingredient of topical skin products, mainly included for its antioxidant properties. Antioxidant levels in the skin are reduced as a result of UV exposure, but vitamin E levels in the stratum corneum have been demonstrated to increase and thus offer protection against lipid peroxidation even upon use of rinse-off products containing only 0.2% alpha-tocopherol or less (Ekanayake-Mudiyanselage *et al.*, 2005). Vitamin E supply to the epidermis and the dermis – is via two routes: penetration of topically applied vitamin E, and via sebum, i.e., the secretion of sebaceous glands, which is high in vitamin E. Therefore, oral supplementation with vitamin E will bolster the skin's antioxidant defences and thus offer photoprotection, especially when given together with its 'antioxidant partner' vitamin C, as has been demonstrated in several human trials (Ekanayake-Mudiyanselage and Thiele, 2006). More recently, specific effects of alpha-tocopherol were discovered in cellular signalling cascades which are also present in photoageing. Alpha-tocopherol inhibits the age-related increase in MMP-1 in vitro (Ricciarelli *et al.*, 1999), and may thus contribute to prevention of photoageing (Fuchs *et al.*, 1989).

Recent meta-analyses have raised concerns about possible adverse effects of supplementation with antioxidants. Specifically, the results of these meta-analyses seem to suggest an overall increased all-cause mortality. However, concerns have been raised as to the validity and relevance of these results, because the studies included in both meta-analyses were extremely heterogenous in terms of study population, antioxidant intervention, co-medication, dosages of antioxidants, study duration and many other aspects. All cause mortality had been chosen as outcome in both meta-analyses, although the quality of the data on all-cause mortality, as well as its definition in the individual trials, is unclear. Further, the relevance of a recent report of an increased risk of skin cancer upon antioxidant supplementation in women (but not in men) needs further evaluation before final conclusions can be drawn, especially since other trials did not observe such effects and because of methodological concerns (establishment of cases, assessment of confounders such as skin type and sun exposure, small number of cases, etc.).

In summary, the meta-analysis and the individual intervention trials reminded us about Paracelsus. However, they do not disregard the overall importance of an optimal supply of nutrients – including antioxidants – for a healthy skin appearance.

17.3.2 Carotenoids

Carotenoids have been studied in relation to sun protection because of their antioxidative properties. Carotenoids are highly efficient scavengers of Reactive Oxygen Species (ROS), particularly singlet oxygen and peroxyl radicals. Peroxyl radicals are generated during the process of lipid peroxidation. Singlet oxygen is produced upon UV-radiation, e.g. in light-exposed tissues such as the skin. Of all naturally-occurring substances, carotenoids are the most efficient

singlet oxygen-quenchers (Stahl and Sies, 2004). Since ROS are generated in the skin by UV-radiation, the sun protective effects of carotenoids were hypothesized and investigated in a number of human trials. In a period of several weeks, oral administration of doses of around 20 mg per day of beta-carotene, as well as of other carotenoids and/or carotenoid mixtures, increase carotenoid levels in the skin and reduce the skin's sensitivity to erythema formation, as demonstrated in several controlled human trials (Gollnick *et al.*, 1996; Stahl *et al.*, 2001; Heinrich *et al.*, 2003; Cesarini *et al.*, 2003; Aust *et al.*, 2005). Combinations of carotenoids, including lutein and lycopene, are as efficient as the same amount of beta-carotene alone and may be preferable in order to avoid concerns about adverse effects of high dose beta-carotene in smokers (Heinrich *et al.*, 2003). Dosage levels as well as duration of supplementation or pre-supplementation are important: only in studies using dosages of about 20 mg carotenoids or higher and supplementing for at least 10 weeks prior to UV exposure were effective. It is assumed that carotenoid levels in the skin remain too low to be protective with administration of lower doses during shorter periods. When beta-carotene was given together with 500 IU vitamin E, reduced erythema sensitivity was observed sooner, and the effect was slightly, but not significantly, greater as compared to beta-carotene alone, thus supporting the 'antioxidant network' concept (Stahl *et al.*, 2000). The effect is not sufficient for protection against extensive sun exposure (sunbathing, etc.).

However, much of the erythemal and sub-erythemal sun exposure over the year occurs outside holiday times, and during daily outdoor activities such as cycling or gardening. Here, systemic sun protection provides a valuable concept in long-term protection against skin damage from solar radiation (Stahl and Sies, 2004). But even during sunbathing, Gollnick found the combination of systemic protection by beta-carotene plus topical application of a sun screen to be more efficient at sun protection than the topical sun screen alone (Gollnick *et al.*, 1996). In addition, oral supplementation of beta-carotene protects against UV-induced suppression of the immune system (Fuller *et al.*, 1992; Herraiz *et al.*, 1998; Gollnick *et al.*, 1996). The consequences of chronic over-exposure to UV-light are skin photoageing or premature ageing of the skin, as discussed above. Here, again, singlet oxygen is involved, in that UVA exposure induces generation of singlet oxygen, which in turn is involved in the regulation of several genes, including those implicated in photoageing such as MMPs. Wertz *et al.* (2004) demonstrated that beta-carotene is able to suppress the UVA-induced upregulation of MMP-1, MMP-3 and MMP-10 by interfering with singlet oxygen-dependent cellular signalling events (Wertz *et al.*, 2004). Consequently, supplementation with an antioxidant combination reduced the expression of MMP-1 and MMP-9 in humans (Greul *et al.*, 2002).

A recent placebo-controlled clinical trial for the first time investigated effects of antioxidant combinations on general parameters of skin health. Thirty-nine healthy volunteers with skin type 2 were randomized to receive placebo or either one of two antioxidant formulations for 12 weeks. Compliance was monitored via serum concentration of the respective antioxidants. The combination of

carotenoids, vitamin E and selenium similarly and significantly improved skin thickness and density, roughness (significant only for formulation B) and scaling from week 0 to week 12, while no changes were observed in the placebo group. Smoothness and wrinkling were unaffected (Heinrich *et al.*, 2006a). Thus, antioxidant nutrients not only provide photoprotection, but also favorably affect skin structure, both of which are modified in skin ageing, as discussed above.

17.3.3 Omega-3 fatty acids

Omega-3 fatty acids are well established for their benefits in heart health, which are probably at least in part related to their anti-inflammatory properties. However, there is accumulating evidence for skin benefits as well. Omega-3 fatty acids are 'polyunsaturated fatty acid (PUFA)', i.e., fatty acids (FA) with at least two unsaturated double bonds. Relevant to human nutrition are long-chain PUFAs (LC-PUFAs), i.e. C18 and longer. Linoleic acid (C18:2 n-6) and linolenic acid (18:3 n-3) are defined as essential FAs, i.e., they cannot be made by the human body itself but must be obtained from the diet. Depending on the position of the first unsaturated double bond from the methyl end of the molecule, PUFAs are categorized into omega-3 (or ω-3, or n-3) and omega-6 (or ω-6, or n-6) FAs. Both are used by the human body as structural components of biomembranes and for the synthesis of the so-called eicosanoids – hormone-like substances which modulate physiological functions. Eicosanoids made from ω-3 FA have weaker and sometimes opposite effects than their counterpart made from an ω-6 FA. Therefore, the ratio between the two is most important.

As in all tissues, the fatty acid pattern of skin lipids is associated with the dietary intake of those fatty acids. Usually, the n-6 fatty acids linoleic acid (LA) and arachidonic acid (AA, C20:4n-6) are the most and second most abundant PUFA in skin (Ziboh *et al.*, 2000). However, upon supplementation with ω-3 FA (fish oils and/or EPA) the concentrations of these fatty acids in skin increase significantly, along with the reduction of pro-inflammatory cytokines such as prostaglandin E_2 (PGE_2) (Rhodes *et al.*, 1995; Shahbakhti *et al.*, 2004). Accordingly, supplementation with ω-3 FA is suggested in inflammatory skin conditions such as atopic dermatitis, psoriasis, and polymorphic light eruption. However, healthy subjects may also benefits from ω-3 FA: as mentioned above, the ratio of ω-6 to ω-3 affects the balance between pro- and anti-inflammatory eicosanoids, and may thus modulate the susceptibility to inflammatory responses, including reactions of the skin ('sensitive skin'). Ratios of 4 : 1 have been suggested as desirable, but are usually between 7 and 17 : 1 in Western countries.

Another local inflammatory reaction of the skin is sun burn (erythema), which occurs upon overexposure to UV-light. Supplementation with 10 g of fish oil (containing 1.8 g EPA and 1.2 g docosahexaenoic acid (DHA)) for 3 months reduced the sensitivity towards erythema formation: after supplementation, more than twice the dose of UV-light was necessary to induce erythema (Rhodes *et al.*, 1995). *In vitro*, EPA inhibited UV-induced MMP-1 expression, thus

suggesting a possible role in ameliorating premature ageing of the skin (Kim *et al.*, 2005).

In addition to effects mediated by eicosanoids, PUFAs themselves have a structural role in skin: Linoleic acid is central in maintaining the integrity of the epidermal water barrier (Ziboh *et al.*, 2000). One of the symptoms of PUFA deficiency are skin lesions and dermatitis, although it is ambiguous whether this attributable solely to a deficiency in ω-3, or a combined ω-3 plus ω-6 FA deficiency (Anderson and Connor, 1989).

Very recent data from a placebo-controlled, double blind intervention trial in 45 healthy women demonstrate improved skin smoothness and reduced redness upon supplementation with omega-3 FA (significant changes after 12 weeks compared to baseline values, no changes in the placebo group), thus contributing to a healthy appearance of the skin.

17.3.4 Plant extracts

Green tea extract

Camellia sinensis L. leaves extract, is rich in catechins, particularly epigallocatechin gallate (EGCG). These are a subgroup of another huge group of secondary plant products: the flavonoids. Owing to their polyphenolic nature, these are highly efficient antioxidants, but have further effects as well. With regard to skin, effects of both topical and oral application of green tea polyphenols have been investigated. Topical application reduced erythema sensitivity and formation of sunburn cells, and protected Langerhans cells from UV-induced damage (Katiyar *et al.*, 2000; Elmets *et al.*, 2001). Similar effects were observed with oral application: erythema formation was reduced, as were general skin damage and lipid peroxidation (Katiyar *et al.*, 2001; Kim *et al.*, 2001).

Grape seed extract

Vitis vinifera L. seed extract, has a high content of polyphenols, including up to 25% OPC (oligomeric proanthocyanidins). OPCs are polyphenols which consist of monomers and dimers of bioflavonoids, with enhanced bioavailability due to a smaller molecule size, and which are powerful antioxidants. Grape seed extract is recommended for body composition formulas because it may limit dietary fat absorption and accumulation of fat in adipose (fatty) tissue (Pinent *et al.*, 2005). It is also thought to help improve and preserve the skin's elasticity by stabilizing collagen and elastin. Grape seed extract is effective for swollen legs or puffiness in the face because it enhances the membrane strength and tissue connection (Constantini *et al.*, 1999).

Cocoa polyphenols

Cocoa polyphenols, extracted from the seeds of the cacao tree (*Theobroma cacao)*, comprise largely flavanols, which form another class of flavonoids. Main flavanol constitutents of cocoa are catechin and epicatechin in monomeric to octrameric form. As discussed for grean tea extract, such flavanols are

efficient antioxidants, but also modulate enzyme activities and display anti-inflammatory effects. Further, vascular effects have been suggested. Recent clinical research demonstrated that chronic ingestion of cocoa polyphenols reduces erythema sensitivity, thus contributing to endogenous photoprotection. Further, cutaneous and subcutaneous blood flow improved, as did skin density and hydration, which, together with the observed increase in skin thickness contribute to overall improved skin appearance (Heinrich *et al.*, 2006a). Improved dermal blood flow was also observed after a single dose of cocoa polyphenols (Heinrich *et al.*, 2006b; Neukam *et al.*, 2007).

17.4 Food applications of skin nutrients

During the product development of a skin supplement or a beauty food product several requirements have to be taken into account. Product composition and positioning is mostly influenced by the regulatory requirements of the target market, which have to be taken into account right from the beginning of the development process. Taste, stability and bioavailability limit the possible combination of ingredients, as well as the number of suitable food matrices. The challenge of a nutritional product with skin benefits is to achieve a final product with the desired sensory and efficacy properties. Very often, aqueous systems are used, such as dairy products or milk-based fruit drinks. In these cases water-soluble plant extracts are easy to formulate but lipophilic functional ingredients such as PUFAs or vitamins are difficult to incorporate. To facilitate the addition of functional lipid components, a variety of powder products have been developed. Very often, spray-dried powders, which are easily dispersible in the aqueous system, are used. The main challenge is to achieve a high active concentration of the active ingredient while maintaining a free flowing powder. In aqueous systems, it is therefore preferable to add the product in an emulsion form. Oils, such as PUFAs, are added to the final product as triacylglycerols. In every case, deodorized products have to be used to ensure good sensory properties of the final product. The oils can be added with the aid of an emulsifier to improve the dispersibility of the oil. However, this may not always be desirable, as the emulsifier will bring additional flavor components to the product. It is necessary to homogenize the product to achieve homogeneous distribution and stabilization of the oil. Usual processing conditions, such as pasteurization, UHT treatment, etc., will not affect the properties of the functional ingredient.

Plant extracts have to be selected carefully because not every plant extract complies with the regulatory and application requirements governing their use in beauty foods. Extracts must have a food status, and this status is differently defined even within Europe. Food status depends on the traditional use of the plant food, the presentation of the product to the consumer, its physiological or pharmacological function, dosage as well as on the manufacturing process of the plant extract. Plant extracts are concentrated preparations usually obtained from

dried-vegetable plant materials. Extraction has to be performed with a food grade solvent, which is allowed for use in the respective category of foods. If the traditional food use of the chosen plant is an infusion, an aqueous extract should be selected, in order to guarantee that the final composition of the extract is similar to the traditionally consumed infusion. Other solvents than water could change the composition to an extent that the resulting extract will be considered a Novel Food according to Directive 258/97/EC. A number of contaminants are regulated in foods, such as heavy metals, mycotoxins, dioxins, PAH and PCB. Depending on the type of food, these contaminants must be carefully monitored. One of the main issues for the future will be to increase the bioavailability of functional ingredients. Poor bioavailability is the result of poor dissolution or low aqueous solubility degradation (poor chemical or enzymatic stability) in gastric or intestinal fluids, further poor intestinal absorption. Therefore, improved solubilisation, enhanced absorption, adequate stability and controlled release of the functional ingredients is required. Nano-structured products or special delivery systems such as molecular encapsulation will be the products of the future. Increased bioavailability, as a consequence requires a careful toxicological re-assessment of the new product as the safety of a food must be guaranteed.

17.5 Future trends and markets

Consumers increasingly expect professional results from skin supplements as well as from cosmetics. There is a trend in Europe for medically endorsed brands in skin nutrition linked to pharmacies as distribution channels. Consumers tend not to believe in foods or beverages for skin support when they contain ingredients which are not generally recognized as healthy. Saturated fatty acids often included in processed foods are associated with poor skin, whereas the opposite is true for foods rich in PUFA and fruit and vegetables (Datamonitor, 2006). Products should communicate the science behind the products simply and effectively, thus enabling the consumer to come to their own decision and select exactly what they consider as a healthy diet. Credibility obtained by adequate information and education of consumers are key topics to be included in strategies in the marketing of future skin care products with proven efficacy. This is in contrast to the marketing of so-called 'wellness' products, with unproven effect on health and wellbeing. With regards to claims, beauty products are not affected by the health claim regulation for food claims. Health claims for food generally are governed by European Regulation 1924/2006/EC, requiring an assessment of the claim by the European Food Safety Authority (EFSA) and formal approval by the Commission. General beauty claims or beauty maintenance claims are not covered by Regulation 1924/2006/EC as they suggest no relationship between a food and health (Art. 3 (4)). They still fall under and have to comply with certain food legislations to be generally safe for public health. Beauty claims must not be misleading, which is an overall

legal requirement in communication addressed to consumers, but they do not need approval prior to use. As a result of the characterization of the human genome and improved understanding of the potential of nutrients to maintain or improve health, our nutrition is more and more personalized, and in future individuals may even be able to identify possible predispositions to diet-related diseases. They may be able to map their individual health-based on information about their individual genetic code and use nutrition as a key factor to maintain or improve their health. However, even if the science is not yet ready to be applied to new nutritional product development, there is a trend to divide consumers into target groups with similar expectations and requirements. For example, in relation to skin health and nutrition, groups may be defined by age or by skin properties such as dry skin or mature skin.

17.6 Sources of further information and advice

Books on skin biology and ageing

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- Gilchrest and Petersen (1996), *Biology of the skin*, ISBN 1-85070-006-0.

Books on nutrients

- Maffei M (2003), *Dietary supplements of plant origin*, Taylor and Francis ISBN 0-415-30835-6.

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18

Nutrition and the metabolic syndrome in the elderly

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Abstract: This chapter focuses on the role of metabolic syndrome (MetS) in the elderly. As MetS is definitely a diet-related syndrome, we will discuss the importance of this syndrome in the elderly as well as the potential for prevention and management by dietary changes specifically in this age-group. This is important, as most evidence on the role of nutrition has been collected on middle-aged populations. As of yet, it is not completely clear to what extent these results can be extrapolated to the elderly, especially to those after 70 years of age with an altered physiology and higher risk of unintended weight loss.

Key words: metabolic syndrome, insulin resistance, elderly, dietary pattern, nutrients.

18.1 Introduction

The cluster of metabolic risk factors for cardiovascular disease, now known as metabolic syndrome (MetS), has received much attention from the medical profession in the past five years. It is definitely appropriate to think about this syndrome as a diet-related disease, and in this chapter we will further discuss the importance of this syndrome in the elderly, and the potential for prevention and management by dietary changes specifically in this age group. This is important, as most evidence on the role of nutrition has been collected on middle-aged populations. As of yet, it is not completely clear to what extent these results can be extrapolated to the elderly, especially to those after 70 years of age with an altered physiology and higher risk of unintended weight loss.

The MetS will be introduced in the first section. Insight into the prevalence of

MetS and its comorbidities in the elderly will be part of the Section 18.2. In the third section extensive attention will be paid to the role of various nutrients in the treatment of MetS. Then the role of dietary patterns and the importance of prevention will be discussed, and in the final part the most prudent dietary advice regarding MetS in the elderly will be formulated.

18.1.1 Origin of MetS

We should refer to Gerald Reaven as one of the founding fathers of research into what he then called 'syndrome X', or later 'the insulin resistance syndrome or metabolic syndrome' in a lecture at the 1988 annual meeting of the American Diabetes Association. He linked insulin resistance of the tissues with hypertriglyceridaemia, low HDL cholesterol and hypertension, in addition to the well-known effect on blood glucose levels, thus underlying both type 2 diabetes as well as coronary heart disease (Reaven, 1988). Somewhat later others included the well-known relationship with (abdominal) obesity in the clustering of risk factors as well, such as in the 'deadly quartet' by Kaplan in 1989.

Since then, various organisations have come up with classification criteria for the insulin resistance or metabolic syndrome (Table 18.1). The research and clinical attention really took off with the publication of the criteria for MetS by the US National Cholesterol Education Program (NCEP) Expert Panel, Adult Treatment Panel-III (ATP-III) (NCEP/ATP-III, 2001). This version includes waist circumference as indicator of abdominal obesity, dyslipidaemia (low HDL cholesterol and/or high triglycerides), elevated blood pressure and elevated blood glucose. As can be seen in Fig. 18.1 the number of publications on this topic has increased dramatically since then, which proves the interest in the MetS from the medical profession.

The American College of Endocrinologists (AACE) later published criteria for what they called the insulin resistance syndrome, focussing on clinical judgement (Einhorn *et al.*, 2003), and in 2005 the IDF published metabolic syndrome criteria including waist circumference with a relatively low cut-off point central in the classification (Alberti *et al.*, 2005) (Table 18.1). Finally, Grundy and co-workers published an update of the ATP-III criteria on behalf of a working group of the American Heart Association/NHBLI in 2005 (Grundy *et al.*, 2005) (Table 18.1).

So far, the 2001 NCEP-ATP-III criteria have been used most, but it can be expected that the revised AHA/NHBLI version (Grundy *et al.*, 2005) will be used more often in the future.

18.1.2 Rationale of MetS diagnosis

The rationale of the NCEP for describing a cluster of cardiovascular risk factors coined the metabolic syndrome was based on recommending LDL lowering medication not only to subjects with high LDL-cholesterol levels, but also for other sub-groups of the general population that have an increased cardiovascular risk.

Table 18.1 Previous criteria proposed for clinical diagnosis of metabolic syndrome

Clinical measure	ATP III (2001)	AACE (2003)	IDF (2005)	AHA/NHLBI (2005)
Insulin resistance	None, but any 3 of the following 5 features:	IGT or IFG, plus any of the following based on clinical judgment:	None	None, but any 3 of the following 5 features:
Body weight (BMI, waist-to-hip ratio, or waist circumference)	Men: waist circumference $\geq$ 102 cm; women waist circumference $\geq$ 88 cm	BMI $\geq$ 25 kg/m^2	Increased waist circumference (population specific) plus any 2 of the following:	Waist circumference $\geq$ 102 cm in men or $\geq$ 88 cm in women
Lipids (high triglycerides, or low HDL-cholesterol or both)	Triglycerides $\geq$ 1.7 mM; HDL-cholesterol <1.03 mM in men or <1.3 mM in women	Triglycerides $\geq$ 1.7 mM; HDL-cholesterol <1.03 mM in men or <1.3 mM in women	Triglycerides $\geq$ 1.7 mM or on TG lowering medication; HDL-cholesterol <1.03 mM in men or <1.3 mM in women or on HDL-C increasing medication	Triglycerides $\geq$ 1.7 mM or on TG lowering medication***; HDL-cholesterol <1.03 mM in men or <1.3 mM in women or on HDL-C increasing medication***
Blood pressure	$\geq$ 130/85 mmHg	$\geq$ 130/85 mmHg	$\geq$ 130 mmHg systolic or $\geq$ 85 mmHg diastolic or on hypertension medication	$\geq$ 130 mmHg systolic or $\geq$ 85 mmHg diastolic or antihypertensive drug treatment in a patient with a history of hypertension
Glucose	>6.1 mM (includes diabetes)*	IGT or IFG (but not diabetes)	$\geq$ 5.6 mM	$\geq$ 5.6 mM or on drug treatment for elevated blood glucose
Other		Other feature of insulin resistance**		

* The 2001 definition was modified in 2004 and from then on used $\geq$ 5.6 mmol/L in accordance with the American Diabetes Association's updated definition IFG (impaired fasting glucose).
** Includes family history of type 2 diabetes, polycycstic ovary syndrome, sedentary lifestyle, advancing age, and ethnic groups susceptible to type 2 diabetes mellitus.
*** Fibrates and nicotinic acid are the most commonly used drugs for elevated TG and reduced HDL-C. Patients taking one of these drugs are presumed to have high TG and low HDL.

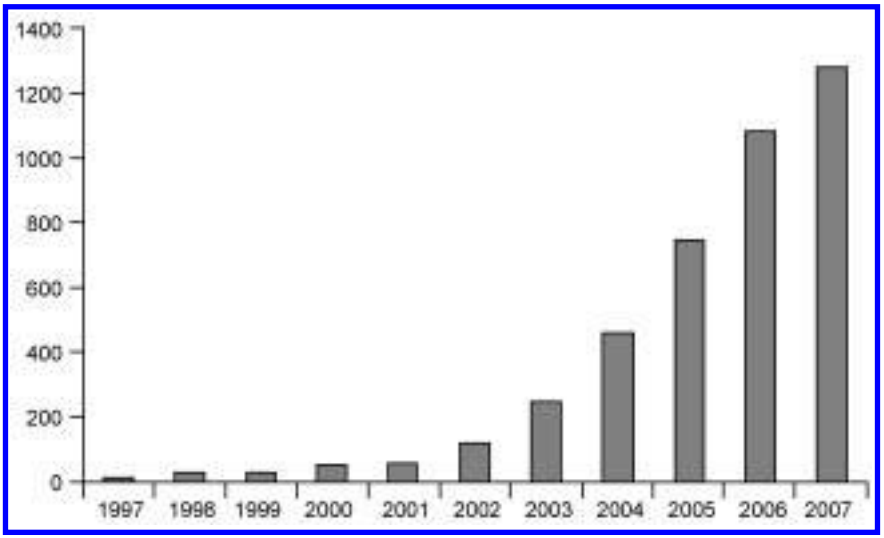

Fig. 18.1 Number of English papers with term metabolic syndrome in the title, PubMed 1990–2006.

In general, the risk for cardiovascular morbidity or mortality is 1.5 to 3 times higher in subjects with the MetS compared to those without (Lakka *et al.*, 2002, McNeill *et al.*, 2005). One should realise, however, that the predictive value of the MetS for myocardial infarction is often not larger, and sometimes even smaller, than the prediction by the Framingham Risk score or the European SCORE function (Wannamethee *et al.*, 2005, Stern *et al.*, 2004). This makes sense, as important CHD risk factors such as LDL-cholesterol are not included in MetS. On the other hand, the MetS indicates that apart from a potentially low (LDL) cholesterol level, there is a group of subjects in the general population that is at increased risk of CVD. This may especially be relevant for the elderly, as the there is uncertainty about the predictive value of elevated LDL-cholesterol at older age (Tikhonoff *et al.*, 2005). In addition, relative risks for the incidence of type 2 diabetes mellitus range from three to seven (Laaksonen *et al.*, 2002a, Sattar *et al.*, 2003).

One can safely say that the focus on abdominal obesity and clustering of risk factors has increased the clinical awareness of obesity as an important risk factor (note obesity is not included in the famous Framingham risk score) and alerted GPs to the presence of other factors as well. But besides increased attention from practitioners and researchers studying the aetiology and possibilities for prevention, severe criticism also appeared (Gale, 2005).

The critique focuses on two issues, the added value of a diagnosis of MetS for clinical treatment, and that for the patient. The critique on the clinical value includes the idea that every risk factor should elicit a search for additional ones, and that the MetS is not special in that, and that treatment should be on any risk factor individually (and aggressively). Grundy eloquently answered these critical remarks (Grundy, 2006). The metabolic syndrome is not a defined

disease but a cluster of risk factors. This cluster does not only include the factors which are used for the classification (glucose, lipids, blood pressure, waist), but also others such as the pro-thrombotic and pro-inflammatory state, and vaso-dilatation. These factors are generally not part of the standard diagnostic measurement set.

In contrast, presence of such a cluster in patients warrants not (only) individual treatment of the risk factors, but (also) lifestyle modification and use of single multi-purpose drugs, to prevent cardiovascular disease and diabetes. This is based on the idea that either insulin resistance and/or abdominal obesity are the main underlying metabolic derangements responsible for the metabolic risk factor cluster. With lifestyle modifications such as weight loss, increased physical activity, and a healthy diet the risk factors can be tackled. The issue of multi-purpose drugs is driven by the challenge of poly-pharmacy. It can be expected that reducing the number of different drugs used by a patient will increase compliance, and by combining different drugs in one multi-purpose one, effectiveness may also be improved.

18.2 Metabolic syndrome in the elderly

18.2.1 Prevalence of MetS changes with age

Regarding the individual components of the MetS, as indicated in Table 18.1, one can easily conclude that the prevalence of most of these factors increases with age, at least to late middle-age. For fasting glucose and blood pressure there is ample evidence of increased levels in older subjects, although for diastolic blood pressure, reductions may occur due to increased vessel wall stiffness (Pinto, 2007). HDL-cholesterol levels tend to decrease into old age (Rhoades *et al.*, 2007), and triglyceride levels are in general higher in older subjects than in younger ones.

For obesity and abdominal obesity this trend may be less clear. Unintended weight loss occurs frequently, and also fat free mass (FFM) may decrease. However, this may affect BMI rather than waist circumference. The decline in BMI especially occurs after age 75 years, whereas simultaneously a redistribution of body fat towards the central part of the body and an increase in waist circumference occurs (Shimokata *et al.*, 1989, Perissinotto *et al.*, 2002).

Insulin resistance, the underlying culprit, also increases with age, although the strong increase of diabetes with age may especially be due to impaired beta-cell sensitivity to glucose and increased impairment to compensate for insulin resistance (Chang *et al.*, 2006). As age increases, several physiological changes occur, such as a decrease in muscle mass, increase in muscle weakness and change within skeletal muscle fibres, leading to a decreased peripheral insulin uptake and insulin resistance.

Despite age-related changes in all of the MetS components, the clustering of these components and the underlying factor hyperinsulinaemia, as marker of insulin resistance, is present in the elderly as well (Feskens and Kromhout,

1994). In the US the data from NHANES III showed that the prevalence of the MetS according to ATP-III criteria increases from 6.7% among subjects aged 20–29 years to 43.5% in subjects aged 60–69 years, and 42% in those of 70 years and older (Ford *et al.*, 2002). In an Irish study the prevalence amounted in men and women from 50–69 years to 24.3% in subjects aged 60–69 years vs. 16.4% in the subjects aged 50–59 years (Villegas *et al.*, 2003).

In the Netherlands the prevalence of MetS amounted to 26% in men and 19% in women of age 50–75 years in the Hoorn study (Dekker *et al.*, 2005) and 25% in a more recent study (Bos, 2007). These data also showed that among subjects younger than 50 years the prevalence of the MetS was higher in men than in women. However, after 50 years, the rates increase in women and became similar, and at older ages the prevalence may be higher in women than in men (Bos, 2007). This fits with the observed changes in abdominal obesity in women after menopause (Misso *et al.*, 2005).

In emerging economies such as India, but also Iran and Turkey, obesity is at younger ages more common in women than in men, and this also holds for the MetS (Ramachandran *et al.*, 2003). The prevalence in the elderly is lower, agreeing with less obesity in these former developing countries. Within the USA and UK several ethnic groups have been studied in detail, such as South Asians and Afro-Carribeans in the UK Southall Study (McKeigue *et al.*, 1991) and Mexican Americans Hispanics and Blacks in the NHANES (US) (Ford *et al.*, 2002). In general one can see that the age-related increase in MetS is steeper in these ethnic groups, with higher rates already at earlier ages.

18.2.2 Associations with disease and co-morbidity

Type 2 diabetes and cardiovascular disease, and notably coronary heart disease, are the main complications of MetS. Few studies have examined the predictive value of the MetS in elderly populations specifically. In the Health, Aging, and Body Composition (Health ABC) study MetS was present in 38% of the 3035 male and female participants aged 70–79 years (Butler *et al.*, 2006). During six years of follow-up coronary events, myocardial infarction, heart failure, and overall hospital stays occurred more frequently in the subjects with MetS, with risk ratios of 1.5.

In the Cardiovascular Health Study (McNeill *et al.*, 2006) 2585 elderly men and women were included, and risk ratios during follow-up were about 1.3 for coronary heart disease, stroke (more for men than for women) and heart failure. The prevalence of MetS amounted to 16% for the ATPIII (2001) criteria and 46% for the ATPIII (2005) criteria. This difference is due to the lower glucose cut-off value in the 2005 criteria. Nevertheless, the risk ratios for disease were similar.

These results show that relative risks are in general lower in elderly than in middle-aged populations. This does not mean that the MetS is less important in the elderly; as rates of co-morbidity increase with age the *relative* excess of cases can decrease, but the *absolute* number of co-morbidity cases with MetS is usually considerably higher in elderly compared to middle-aged populations.

The consequences of MetS, type 2 diabetes and CVD, are also important clinical conditions linked to vascular dementia and Alzheimer's disease. These are the two most common subtypes of dementia in the elderly, and thus the MetS may be a sub-clinical condition that also increases the risk of dementia.

Indeed, we observed an association between impaired glucose tolerance and hyperinsulinaemia, a marker of insulin resistance in non-diabetics, and cognitive function in elderly men from the Zutphen Elderly Study (Kalmijn *et al.*, 1995). Men in the highest category of fasting insulin levels had the best MMSE score, and a 24% excess risk of making errors in the MMSE test. As this study was done in mostly independently living elderly, clear dementia was not found, and these results refer to cognitive decline.

Carantoni and co-workers (2000) showed that non-diabetic patients with vascular dementia had higher fasting glucose and insulin levels than healthy control subjects. In a prospective study on Japanese-American Elderly men followed for 25 years a combination of metabolic syndrome components was associated with an increase in vascular dementia but not in Alzheimer's disease (Kalmijn *et al.*, 2000). This indicates that especially the vascular form of dementia can be affected. However, recently Craft (2006) reviewed the more physiological evidence. He concluded that insulin seems to play a key role in cognition and other aspects of normal brain function. Insulin resistance induces chronic peripheral insulin elevations, reduces insulin activity, and reduces brain insulin levels. Raising plasma insulin to levels that characterise patients with insulin resistance invoked increases in levels of beta-amyloid and inflammatory agents, possibly impairing memory and inducing Alzheimer's disease.

A related observation may be the recent report that MetS is associated with depression. In both men and women, the MetS was associated with an increased prevalence of depression independent of age, smoking status, socioeconomic factors, and lifestyle, and observed across body mass index categories (Skilton *et al.*, 2007). This may partly be due to an underlying association with dementia, but is in any case an interesting area to follow in the future.

Finally, there is now an upcoming hypothesis that insulin resistance and MetS also act as important biological components of some clinical aspects of the frailty syndrome in aging individuals (Abbatecola and Paolisso, 2008). Other MetS related conditions are less specific for the elderly, such as heart failure, sleep apnoea, non-alcoholic fatty liver disease, but also possibly cancer (Ahmed *et al.*, 2006) and overall reduced quality of life (Ford and Li, 2008).

18.3 Nutrition and the treatment of metabolic syndrome

As of yet evidence on dietary interventions on MetS specifically in the elderly is scarce. However, an important example is the large TONE study (Trial of Non-pharmacological Interventions in the Elderly, reported in 1998) that concluded that reduced sodium intake and weight loss constitute a feasible, effective, and safe non-pharmacological therapy of hypertension in older persons (Whelton *et*

al., 1998). This suggests that healthy elderly are by no means different from middle-aged subjects in the response on dietary changes. Of course, for frail elderly this situation may be somewhat different, but so far little data are available on this in the context of MetS.

18.3.1 Weight loss

Is has been shown that correction of overweight can improve all components of the MetS. As the majority of patients with MetS have overweight it should in general be a primary objective of the treatment of the MetS (Riccardi and Rivellese, 2000). The two basic concepts are: dietary modification to avoid weight gain and induce weight loss, combined with increased physical activity in daily life.

But as also indicated in other chapters of the book (e.g., Chapter 3), the treatment of obesity in elderly subjects is topic of controversy (McTigue *et al.*, 2006). Food restraint may lead to malnutrition, to adverse effects on muscle and bone or clear sarcopenia, and the optimal BMI for may be higher than for adults (see also Chapter 3). For example, the link between obesity and morality reduces with ageing and may be absent in subject aged 75 years or older. In a follow-up of the Oslo Diet and Exercise study Holme and co-workers showed that repeated number of episodes of weight loss after age 50 is associated with increased risk of MetS (Holme *et al.*, 2007).

On the other hand, McTigue and co-workers also showed that in elderly subjects intensive counselling strategies incorporating behavioural, dietary, and exercise components promote a weight loss of 3 to 4 kg over a period of 3 years. The weight loss was linked with improved glucose tolerance, improved physical functioning, reduced incidence of diabetes and a combined hypertension and cardiovascular endpoint, and reduced bone density. Regarding the metabolic risk factors, these results are quite similar with those reported by interventions in younger populations (Mensink *et al.*, 2003a), and this fits with observational results on lifestyle and MetS in elderly men (Wannamethee *et al.*, 2006).

18.3.2 Dietary fat versus dietary carbohydrate reduction

Traditionally, recommendations for weight and long-term weight maintenance focused on low-fat high-carbohydrate diets. Astrup and co-workers showed in a meta-analysis that reducing fat intake without intentionally lowering energy intake resulted in greater weight loss than high-fat diets (Astrup *et al.*, 2000). However, this issue is debated, and, for example, an overview of six trials in overweight and obese subjects showed no effect of a low-fat diet after 6, 12 or 18 months (Pirozzo *et al.*, 2003).

Recently, the long-term results of the large US Women's Health Initiative (WHI) were reported (Howard *et al.*, 2006). This major intervention study including ~49 000 women aged 50–79 years showed that women on a low-fat diet reduced weight in the first year of the study (−2.2 kg). Although a gradual

increase took place thereafter until the end of follow-up after 7.5 years, they remained having a modestly lower weight (−0.4 kg) compared with the control group. No differential effects according to age were reported.

Hence, the efficacy of a low-fat diet remains debated. The main discussion points are: what should be the replacement for fat, what type of carbohydrates should be used, what is the impact on abdominal obesity instead of overall weight loss, and what are the effects on the other components of the MetS.

Regarding the latter, indeed a major problem with low-fat high-carbohydrate diets is the effect on serum triglycerides and HDL-cholesterol. Typically, a high carbohydrate diet increases triglyceride levels and reduces HDL-cholesterol (Reaven, 2005, Krauss and Dreon, 1995). This also depends on the source of carbohydrates, and using more complex carbohydrates as recommended, with a concomitant increase in dietary fibre, in general reduces the serum lipids but also HDL-cholesterol levels (Yu-Poth *et al.*, 1999).

The interest of low-carbohydrate diets is therefore gaining. Such a diet typically consists of < 100 g/d or < 30 energy-% of carbohydrate. Nordmann and co-workers recently carried out a meta-analysis of five trials (Nordmann *et al.*, 2006). They indeed showed that low-carbohydrate diets decrease triglyceride levels and increase HDL-cholesterol levels, compared with low-fat diets that reduced total and LDL-cholesterol. In a one-year trial a low-calorie, high-carbohydrate low-fat diet (conventional) was compared with a low-carbohydrate high-protein, high-fat diet ('Atkins diet') (Foster *et al.*, 2003). At the end, no difference in weight loss was seen, but the Atkins type of diet was associated with greater improvement in some MetS components such as HDL-cholesterol and triglycerides. The high protein and calcium intake in a low-carb diet might, however, reduce kidney function, and a high saturated fatty acid intake would increase LDL-cholesterol. Carbohydrates should therefore preferably be replaced by fatty acids that do not increase LDL-cholesterol and do not reduce HDL-cholesterol, such as mono-unsaturated fatty acids (Mensink *et al.*, 2003b).

18.3.3 Carbohydrates, GI and fibre

Besides type of fatty acids, the type of carbohydrate and its associated dietary fibre component is also important. The glycaemic index (GI) is used to quantify the relative effect of carbohydrate-rich foods on post-prandial glucose response, and the glycaemic load (GL) estimates the total glycaemia burden to the body (amount of carbohydrates multiplied by their GI).

A review published in 2003 shows that low-fat high-carbohydrate diets rich in dietary fibre have beneficial effects on several components of the MetS (Davy and Melby, 2003). Beneficial effects of dietary fibre on insulin resistance are supported by results from epidemiological surveys (Feskens *et al.*, 1994, Ylonen *et al.*, 2003), and beneficial effects on blood pressure by a recent meta-analysis of placebo controlled trials (Streppel *et al.*, 2005). Soluble fibre especially has been shown to reduce total and LDL-cholesterol levels and also glycaemic

control in type 2 diabetic patients (Brown *et al.*, 1999) (Chandalia *et al.*, 2000), whereas the insoluble type of fibre has been shown to reduce insulin resistance in obese subjects (Weickert *et al.*, 2006).

A related topic is the role of whole grain products. The use of whole grain contributes to a lower GI and provides fibre and other nutrients, such as lignans, plant stanols and sterols, and vitamins and minerals. Indeed, a study in overweight subjects showed that compared to a 6-wk refined grain diet a similar whole grain diet period reduced insulin resistance (Pereira *et al.*, 2002a), although others were recently not able to confirm this (Andersson *et al.*, 2007).

The GI and GL have gained increasing interest lately, and in several countries such as Australia and UK low GI can now be identified by consumers from the food label. GI and GL lave been clearly related to reduced risk of type 2 diabetes, and have also been suggested to reduce risk of coronary heart disease and to reduce weight loss (Du *et al.*, 2006). Fluctuations in plasma glucose and insulin levels occurring with high GI diets may stimulate hunger and inhibit fat oxidation (Brand-Miller *et al.*, 2002). A recent trial demonstrated that a low-GI diet was able to increase body fat loss and LDL cholesterol (McMillan-Price *et al.*, 2006). However, the effect of GI on glucose metabolism seems to be the most consistent mechanism in the potential effect on MetS.

18.3.4 N-3 fatty acids

High doses of long-chain n-3 fatty acids such as DHA, DPA and EPA occurring in fish oil, reduce plasma triglycerides in hypertriglyceridaemic patients. Also the atherogenic small dense LDL particles are reduced (Rivellese *et al.*, 2003). Other potential beneficial effects on components of the MetS include an increase in plasma HDL-cholesterol, improvement in endothelial function and a reduction of high blood pressure (Carpentier *et al.*, 2006), although the effect on blood pressure is generally small (Geleijnse *et al.*, 2002). N-3 fatty acids may also play a role in reducing inflammation, another partner of the MetS, and by direct or indirect mechanisms they can result in anti-inflammatory effects (Calder, 2006). It has already been known for a long time that fish oil and long-chain n-3 PUFA intake affect thrombosis and haemostasis, such as fibrinogen and PAI-1, which are also associated with MetS (Feskens and Kromhout, 1994).

18.3.5 Dietary protein and dairy

Until recently protein intake has largely been ignored in the debate on the optimal diet for weight loss and treatment and prevention of MetS. However, as it is potentially more satiating, it has achieved more attention as part of the low-fat diets.

In a cohort study dairy use was associated with increased incidence of all components of the MetS, albeit in overweight subjects only, not in the normal weight ones (Pereira *et al.*, 2002b). In a French cross-sectional study MetS was diagnosed more frequently in subjects with low dairy consumption (Mennen *et*

al., 2000). Compared to a high-carbohydrate low-fat diet, a high-protein low-fat diet was shown to reduce serum triglycerides more, while weight loss was similar (Noakes *et al.*, 2005). MacMillan-Price *et al.* tested two high-protein diets. Overall, the highest weight loss occurred in the high-protein/high-GI group, the group with, unfortunately, also the largest increase in LDL-cholesterol (McMillan-Price *et al.*, 2006). Note that with high-protein diets on the short-term kidney function can be compromised (Bernstein *et al.*, 2007). Long-term effects are not yet clear.

Zemel suggested that especially the role of dairy and calcium is important in obesity. Calcium may attenuate body fat accumulation and weight gain during periods of over-consumption of an energy-dense diet, and may increase fat breakdown and preserve metabolism during caloric restriction, thereby markedly accelerating weight and fat loss (Zemel, 2004). In addition, other factors present in dairy may have some additional effects, possibly due to additional bioactive compounds such as angiotensin converting enzyme (ACE) inhibitors in dairy, as well as the rich concentration of branched chain amino acids, which act synergistically with calcium to attenuate adiposity (Zemel, 2004). These branched chain amino acids may also have an insulinotropic effect (Pfeuffer and Schrezenmeir, 2007), stimulating insulin secretion and resulting in the relatively low GI of diary products (Foster-Powell *et al.*, 2002). Low-fat dairy has also been shown to reduce blood pressure levels (Pfeuffer and Schrezenmeir, 2007). The exact underlying mechanism is still now known, although ACE-like peptides may play a role in addition to the high calcium content.

18.3.6 Micronutrients

Micronutrient deficiencies in the elderly may refer to vitamin B-12, vitamin A, vitamin C, vitamin D, calcium, iron, zinc, and other trace minerals, especially when energy intake is too low. For some, such as the vitamins C and D, calcium (see above) and iron, a role in MetS can be envisaged.

For example, part of the effects of dairy and fatty fish could have been due to their vitamin D content. The large Women's Health Initiative, which included older women, recently reported that calcium plus cholecalciferol supplementation had an effect on the prevention of weight gain, primarily in women who reported inadequate calcium intakes at baseline. Earlier, low vitamin D levels were shown to be associated with high post-load glucose levels and hyperinsulinaemia (Baynes *et al.*, 1997). A recent systematic review and meta-analysis concluded that vitamin D and calcium insufficiency may negatively affect glycaemia, whereas combined supplementation with both nutrients may be beneficial in optimising glucose metabolism (Pittas *et al.*, 2007).

Also, the beneficial effects of dietary fibre may be partly due to concomitant increase of a micronutrient, in this case magnesium. Magnesium has been shown to reduce blood pressure (Jee *et al.*, 2002). It was also associated with a reduced risk of type 2 diabetes in two large cohorts from Harvard University (Lopez-Ridaura *et al.*, 2004) and with MetS in young adults (He *et al.*, 2006). In general,

magnesium appears to be important in glucose metabolism (Barbagallo and Dominguez, 2007). However, magnesium, calcium and potassium intakes are generally correlated and careful statistical analysis is needed to disentangle the associations.

Sodium is an important mineral for MetS as well. Although long debated, there now appears to be consensus in the field of public health nutrition that sodium intake is too high and should be reduced to limit the risk of hypertension (Myers and Champagne, 2007, Adrogue and Madias, 2007). Partial replacement by potassium and magnesium salts seems therefore to be a good option, not only to reduce blood pressure but also insulin resistance. However, keeping or even improving the taste of foods and meals is essential in frail elderly to help restore appetite.

In contrast, the antioxidant hypothesis has received some serious setbacks in the past few years. Large, long-term placebo controlled trials showed no reduction in cardiovascular disease or diabetes (Liu *et al.*, 1999, Liu *et al.*, 2006). On the other hand, intakes of antioxidants such as vitamin E, vitamin C and carotenoids were been associated with components of MetS in several epidemiological surveys (Feskens *et al.*, 1995). Also, body iron stores, promoting oxidative stress, have been associated with increased risks of type 2 diabetes and were higher in Italian MetS subjects than in controls (Forouhi *et al.*, 2007, Bozzini *et al.*, 2005). These contradictory findings indicate that a clear role for antioxidants in the treatment of MetS is so far not indicated. This holds for all ages.

18.3.7 Alcohol use

The U-shape relationship between alcohol consumption and CHD, and also HDL-cholesterol, indicating the most beneficial effects with moderate alcohol use, is well known (Sesso, 2001). However, to what extent this information can be used in a treatment guideline for MetS also depends on other issues, such as the risk of other diseases, such as cancer and liver disease, violence and accidents, and specifically in the elderly co-morbidity and the issue of polypharmacy (see Chapter 22). It should be stressed that the HDL-cholesterol-lowering effect of alcohol is only seen for moderate intake, not for high alcohol use. In addition, there exists a graded positive association between alcohol use and blood pressure, although the contribution of alcohol to hypertension in the general population is lower compared to overweight and the minerals Na, K and Mg (Geleijnse *et al.*, 2004). Moderate alcohol intake has also been associated with reduced diabetes incidence in several studies (Carlsson *et al.*, 2005), but the marker for alcohol abuse γ-glutamyltransferase (GGT) is a risk factor for type 2 diabetes and MetS in the French DESIR study, confirming a less beneficial role of the liver as well (Andre *et al.*, 2007). Again, the dose of ethanol may play an important role in determining the balance between positive and negative effects.

18.3.8 Physical activity

Although a bit beyond the scope of this chapter, some words on the role of physical activity in the treatment of MetS are warranted. Exercise is important for the elderly for the maintenance of lean body mass (see Chapter 10). Although most evidence of a beneficial effect of exercise in MetS is derived from studies on weight loss and accompanying metabolic changes, increase in muscle mass may especially be helpful in elderly patients, as sarcopenia has also been associated with several features of the MetS (Hurley and Roth, 2000). Muscle is an important determinant of insulin resistance, fatty acids metabolism and resting energy expenditure.

A recent Cochrane review shows that both low calorie and low-fat diets are more effective in facilitating weight loss than exercise alone (Shaw *et al.*, 2006). When combined with exercise, diet resulted in a greater weight reduction than diet alone (−1.1 kg). Increasing exercise intensity also increased the magnitude of weight loss (−1.5 kg). Further evidence of the role of physical activity in the prevention of MetS can also be derived from epidemiological studies. Finnish men who engage in moderate- to high-intensity leisure-time physical activity had a 50% reduced risk of developing MetS during four years of follow-up (Laaksonen *et al.*, 2002b), and this effect may even be independent of $VO_{2max,}$ i.e. physical fitness (Ekelund *et al.*, 2005).

Most of these studies used aerobic training and until recently most of the recommendations on physical activity focused on vigorous aerobic exercise. More recent evidence comes from trials and observational studies which showed that brisk walking and other form forms of moderate-intensity activity may be effective as well (Jakicic *et al.*, 2003). This may be especially relevant for the elderly. Inclusion of moderate to light activities in a large-scale diabetes prevention programme (DPS) was associated with reduced risk of diabetes (Laaksonen *et al.*, 2005), indicating its promise.

18.4 Diet and the prevention of metabolic syndrome (MetS)

In the preceding section we focussed on the individual nutrients and the treatment of MetS. In this section we will expand on prevention of the Mets, including dietary patterns instead of single nutrients. In fact, the dietary factors which play a role in the treatment of MetS are exactly the same as those that should be involved in the prevention of the syndrome. Hence the information from the preceding paragraph need not to be repeated and this section will focus on foods and dietary patterns.

As people in general do not eat nutrients but foods, and choices are made within a daily pattern, the dietary pattern is of great importance in practice. Also the combination of various nutrients can play an additional role in the efficacy of prevention, as small effects of single nutrients can be summed, and sometimes even can interact positively thus strengthening each other.

18.4.1 Dietary patterns and MetS

Studies on dietary patterns in relation to morbidity and mortality have been carried out for about 10–15 years. In general, the information on the nutrients and foods is summarised into a smaller number of factors, which are subsequently related to outcome. These factors can be pre-determined, such as food quality indices (Waijers *et al.*, 2007), or can be based on the correlation structure of the data at hand using factor analysis or cluster analysis. Dietary quality scores were for example associated with survival and risk of cardiovascular disease or cancer (Huijbregts *et al.*, 1997, Knoops *et al.*, 2006, Trichopoulou *et al.*, 2003). Using factor analysis a so-called cosmopolitan food pattern was associated with lower blood pressure and higher HDL-cholesterol concentrations, and a traditional pattern score was associated with higher blood pressure, and higher concentrations of HDL-cholesterol, total cholesterol and glucose (van Dam *et al.*, 2003).

Baxter *et al.* (2006) concluded in a recent review that no individual dietary component could be responsible for the association between diet and MetS. However, the quality of the diet, as often expressed in a form of dietary pattern, was clearly important. Of all the food groups studied, whole grain products appeared to have the most consistent inverse association with MetS.

Several additional studies were reported after publication of this review. Using cluster analysis, grouping subjects rather than variables, three dietary patterns were identified in an Irish study (Villegas *et al.*, 2004). The 'prudent diet' group had the lowest score for insulin resistance compared to the 'traditional Irish diet' group and the 'high alcohol and convenience food' group. In the US Framingham Offspring-Spouse Study five non-overlapping dietary patterns emerged, characterised as heart healthier, lighter eating, wine and moderate eating, higher fat, and empty calories. The prevalence of MetS was highest in the empty calorie group (Sonnenberg *et al.*, 2005). When in the same study nutritional risk was defined based on 19 nutrients, the development of MetS during 12 years of follow-up was most strongly related to the high composite nutritional risk, characterised by higher fat, saturated fatty acids intake, higher alcohol use and lower intake of fibre and micronutrients (Millen *et al.*, 2006). Also in another US cohort a so-called Western dietary pattern was associated with increased risk of MetS during follow-up (Lutsey *et al.*, 2008). A Greek study showed that a dietary pattern that includes cereals, fish, legumes, vegetables and fruits was associated with reduced levels of MetS features, whereas meat and alcohol showed the opposite results (Panagiotakos *et al.*, 2007). In a study of women from Teheran, three major dietary patterns were identified using factors analysis. The prevalence of MetS was lowest in the highest score of healthy diet pattern, Western diet was positively associated with MetS (Esmaillzadeh *et al.*, 2007). The Mediterranean diet score was inversely associated with MetS in a Spanish cohort indicating higher rates of MetS in men and women with the least Mediterranean diet type (Tortosa *et al.*, 2007).

In summary, all of these data suggest that a dietary pattern known as a 'prudent diet' is associated with the development, or presence, of MetS. Studies

specifically focusing on elderly men or women are so far lacking, although a recent review for example concluded that the Mediterranean dietary pattern was associated with increased healthy ageing (Roman *et al.*, 2008).

18.4.2 Dietary interventions and MetS

Recently, several intervention studies investigated the impact of a healthy dietary pattern on the development of MetS or its components. Three major dietary patterns were investigated: a general healthy dietary pattern according to the local guidelines, a Mediterranean dietary pattern, and the so-called DASH-diet (Dietary Approaches to Stop Hypertension).

Two landmark studies showed that type 2 diabetes can be prevented by a healthy lifestyle, i.e. adhering to a healthy diet and increasing physical activity. In both cases the healthy diet consisted of a reduction in saturated fatty acids to ~30 energy%, and an increase in fibre intake, as well as a reduction in body weight. The *Finnish Diabetes Prevention Study* (DPS) showed that the four-year intervention even succeeded in a sustained reduction of diabetes risk after discontinuation of the study (Lindstrom *et al.*, 2006). The *US Diabetes Prevention Project* (DPP) showed that the lifestyle intervention was even more effective in reducing diabetes risk in subjects with impaired glucose tolerance compared to drug treatment with metformin (Diabetes Prevention Program Research, 2002). A smaller Dutch study using the DPS protocol was shown to reduce 2-hr blood glucose levels by 1 mmol/L despite of a moderate weight reduction of 2.3 kg (Mensink *et al.*, 2003a). However, in this relatively small study (total 147 subjects) other components of the MetS were generally not reduced. Instead, Esposito and co-workers showed a clear benefit on MetS and it components using a Mediterranean diet advice (Esposito *et al.*, 2004). They included 180 Italian patients with MetS, and randomised half of the group to receive detailed dietary advice to increase daily consumption of whole grains, fruits, vegetables, nuts, and olive oil. The control group followed a so-called prudent diet, carbohydrates 50–60 energy-%, proteins 15–20 energy-%; total fat < 30 energy-%. After two years mean body weight reduced more in the intervention group (−4.0 kg) than in the control group (−1.2 kg). Also, they had lower concentrations of CRP and several cytokines in plasma, and lower insulin levels. Endothelial function improved. Finally, 56% of the intervention subjects had regressed to normal, compared to only 13% in the control group, indicating that MetS was successfully treated.

In the French *Medi-Rivage study* 212 volunteers with CVD risk factors were randomised to a Mediterranean type of diet or a low-fat diet instruction (Vincent-Baudry *et al.*, 2005). After three months both diets appeared to reduce MetS components such as triglycerides and insulin, but not blood pressure. In Spain the *PREDIMED study* recently reported the results on 770 subjects at risk for CVD after three months of intervention (Estruch *et al.*, 2006). Participants were assigned to a low-fat diet or to one or two Mediterranean diets, consisting of nutrition education and either free virgin olive oil or nuts. Compared to the

low-fat diet, the two Mediterranean diets reduced plasma glucose and insulin, and blood pressure, and increased HDL-cholesterol. The olive oil version also reduced CRP levels, and the nuts version reduced triglycerides and total cholesterol as well.

Regarding blood pressure the *Dietary Approaches to Stop Hypertension (DASH) trial* is the most noteworthy. Its main results were published in 1997 (Appel *et al.*, 1997). This diet emphasises fruits, vegetables and low-fat dairy products. It includes whole grains, poultry, fish and nuts, and is reduced in fat, red meat, sweets and sugar-containing beverages. Among subjects with normal blood pressure this diet reduced systolic blood pressure by 3.5 mmHg and diastolic blood pressure by 2.1 mmHg. In hypertensive subjects the reductions were even larger, 11.4 and 5.5 mmHg respectively.

In the subsequent *PREMIER trial* a combination of weight loss, sodium reduction, increased physical activity and the DASH diet, was tested (Appel *et al.*, 2003). Compared to control approach reductions in systolic blood pressure were 6.3 mmHg in hypertensives and 3.1 mmHg in subjects with normal blood pressure.

In summary, intervention studies have also indicated the potential for a healthy diet in reducing MetS features and in preventing MetS. However, only the Italian study of Esposito addressed the prevalence of MetS directly. A main question in this study is whether the beneficial effects have been due to the impact on body weight or body fat distribution, or were independent of changes in weight or caloric intake.

18.5 Conclusions

The MetS is highly prevalent, especially in middle-aged to older subjects. With the current obesity epidemic and ageing of the populations, both in the developed and developing countries, the number of subjects with MetS will steadily increase. As important risk factor for type 2 diabetes, cardiovascular disease and possibly related outcomes such as stroke, vascular dementia and Alzheimer's disease, and depression, both treatment and prevention is warranted. Special attention should also be paid to the suggested impact on sarcopenia and frailty.

Diet should be a cornerstone in management and together with physical activity is the most important preventive factor. Luckily, the MetS components have many dietary determinants in common. It can be summarised that a diet *high* in fruit and vegetables, whole grains and fibre, and *low* in saturated fatty acids and sodium, and *moderate* in monounsaturated fatty acids, fish and alcohol, would reduce all of the MetS components (Table 18.2).

However, several uncertainties still exist, and need to be investigated further. A main issue on MetS in the elderly is the role of weight loss and caloric restriction. For otherwise healthy subjects it is clear that weight reduction is important, as generally 80% of the MetS cases are overweight. Energy

Table 18.2 Dietary recommendations for the different components of MetS (based on Feldeisen and Tucker, 2007, and WHO/FAO report Diet and the prevention of chronic diseases, 2003)

MetS component	Dietary recommendation
Abdominal/central obesity	Healthy dietary pattern Reduced caloric intake (but monitor anorexia of ageing in the elderly) Low saturated fatty acids and trans fatty acids High fruit, vegetable, whole grain, fibre
	Convincing according to WHO/FAO 2003 report: a high intake of dietary non-starch polysaccharides (NSP)/fibre, and a low intake of energy-dense, micronutrient-poor foods
High blood pressure	DASH diet Reduced sodium, replace by potassium and magnesium salts Low to moderate alcohol
	Convincing according to WHO/FAO 2003 report: low sodium high potassium diet
Dyslipidaemia	Reduced caloric intake if weight loss is needed Mediterranean diet: low saturated fatty acids and trans fatty acids, high fruit, vegetables, whole grain, fibre; moderate fat from unsaturated origin (MUFA) Moderate fish Low to moderate alcohol
	Convincing according to WHO/FAO 2003 report: low trans fatty acids and moderate alcohol use for increasing HDL-cholesterol, triglycerides are not specifically addressed
High glucose	Reduced caloric intake Mediterranean diet: low saturated fatty acids and trans fatty acids, high fruit, vegetables, whole grain, fibre; moderate fat from unsaturated origin (MUFA) Moderate fish Low to moderate alcohol
	Probable according to WHO/FAO 2003 report: low saturated fatty acids and high non-starch polysaccharides/fibre diets

restriction is then part of the approach. However, in the elderly the risk of anorexia of ageing needs to be avoided, and the situation in frail elderly may be complex. Micronutrient deficiencies need to be avoided as well. Hence, it should be proposed that reduced caloric intake is used only when needed in case of overweight and absence of risk of involuntary weight loss and deficiencies. More evidence on the role of the proposed diet in the treatment and prevention of MetS in the elderly would be welcome.

Other uncertainties are more general for MetS. The role of several individual nutrients or dietary components remains to be elucidated, and their underlying mechanisms need to be unravelled before any firm specific recommendations can be made. This refers, for example, to micronutrients and protein.

This is a challenge, but successful interventions are needed in face of the increasing number of subjects with MetS which we are expecting in the near future.

18.6 References

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19

Fat-soluble vitamins and ageing

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Abstract: Ageing has long-been attributed to accumulation of biological molecules damaged by continuous exposure to oxygen-derived reactive species. Oxidative stress has also been associated with many physio-pathological features occurring together with biological ageing including skin wrinkles, eye-diseases, osteoporosis, neurological disorders and cardiovascular disease. Presently, in Western countries more and more people are concerned with the issue of delaying the ageing processes. Epidemiological observations clearly indicate that diet and lifestyle may help to prevent age-related diseases. Laboratory investigations also show the presence of healthy components in the non-energetic moiety of the diet. Among them, it has long been proposed that fat-soluble vitamins might play an important role to counteract some of age-related disorders. The present review will focus on the dietary sources, bioavailability and functions of vitamin D, vitamin K, vitamin A/pro-vitamin A carotenoids and vitamin E.

Key words: elderly, tocopherol, cholecalciferol, ergocalciferol, retinol, phylloquinones, menaquinones.

19.1 Introduction

What is common to all mammals including human beings is the use of molecular oxygen for reactions that bring the necessary energy for physiological processes. During these processes oxygen molecules are metabolized into unstable super-oxide anion characterized by the presence of a supplementary electron. To gain stability, the electron is transferred into other molecules and this chain reaction results in highly reactive free radicals, able to propagate, and to chemically and functionally modify all biomolecules. Lifelong exposure to oxygen may then stochastically lead to such modifications at more or less great extent. Therefore the ageing process has long been attributed to the accumulation of damages induced by oxygen-derived reactive species (Harman, 1956).

On the other hand, ageing is a subtle combination of physiological (healthy ageing) and pathological processes, linked together. A simple observation on biological parameters clearly shows significant differences according to age. An increasing blood cholesterol level is one of the most well known biological parameter changes with age (Schaefer *et al.*, 1995). Others, including albumin and to a lesser extent thyroid hormone appear to decrease with age in otherwise healthy individuals as studied in the Vitage study (Rock *et al.*, 2001). Similarly, physiological data also show age-related changes with appearance of clinical signs in a more or less lengthy delay. Body mass index and blood pressure were repeatedly shown to increase with age, independently of occurrence of pathologies. Cutaneous and eye ageing are other physiological manifestations in the elderly with skin wrinkles and opalescent lens both of which were supposed to be consecutive to exposure to ultraviolet light and air oxygen leading to oxidative stress. Therefore longer time exposure to free radicals and biological changes in elderly might also explain why, compared to young individuals, elderly people are usually characterized by one or more of the following diseases, atherosclerosis, cancer, osteoporosis, eye diseases or dementia. This observation means that ageing increases vulnerability to all age-associated pathology (Hayflick, 2007).

As population age increases in Western countries, more and more people are concerned with the issue of delaying the ageing process. Among many determinants, nutrition has been designed as a means to preserve health during ageing. Through epidemiological observations, it was attempted to define the healthy diet, whereas laboratory investigations aimed at defining healthy components of the diet. Globally, a diet can be divided into energetic and non-energetic moieties. The latter includes mineral and trace element, vitamins, polyphenols and carotenoids. Among many other components of the diet, fat-soluble vitamins have long been suspected as being essential for preserving health status as the organism ages, because of their functions that may act within the processes at the genesis of the previous mentioned diseases. In the present chapter, updated data will be provided on vitamins, focusing on fat-soluble vitamins, i.e. vitamin D, vitamin K, vitamin A/pro-vitamin A carotenoids, and vitamin E. Each of these nutrients will be addressed in relation to age-related diseases and discussed in view of their dietary sources. bioavailability and functions. The mechanisms recently demonstrated at the cell and molecular level will also be presented in order to show the complex relationship between fat-soluble vitamins and nutrition of the elderly. Chemical structures and features of these fat soluble vitamins are shown in Table 19.1 and Fig. 19.1.

19.2 Vitamin D

Cholecalciferol and ergocalciferol are the two forms of vitamin D. Vitamin D is not strictly a vitamin since it can be synthesized by the body. Therefore, vitamin D needs can be met by both dietary intake and endogenous synthesis by sun

Table 19.1 Fat-soluble vitamins and nutrition of elderly

	Chemical name	Dietary sources	Particularity	Deficiency signs	Preventive effect	Normal plasma level	Daily intake level
Vitamin D	Cholecalciferol Ergocalciferol	Fatty fishes Dairy products	Sun exposure induces endogenous synthesis	Rickets Osteomalacia	Bone loss	30–40 ng/mL	15–20 μg
Vitamin K	Phylloquinone Menaquinone	Dark leafy vegetables Herbs	Carboxylation of osteocalcin	Hemorragia anemia	Bone health	1–2 ng/mL	90 μg
Vitamin A	Retinol Retinal Retinoic acid	Liver Yellow-orange fruits and vegetable	Provided by pro-vitamin A carotenoids	Xerophtalmia (eye) Hyperkeratosis (skin)	Infectious disoders	> 300 μg/mL	700–900 μg
Vitamin E	Tocopherol Tocotrienol	Vegetable oils (sunflower and palm)	Antioxidant and non-antioxidant functions	Hemolytic anemia Myopathy Retinopathy	Cardiovascular disease Cancer (prostate)	12 μg/mL	20–50 μg

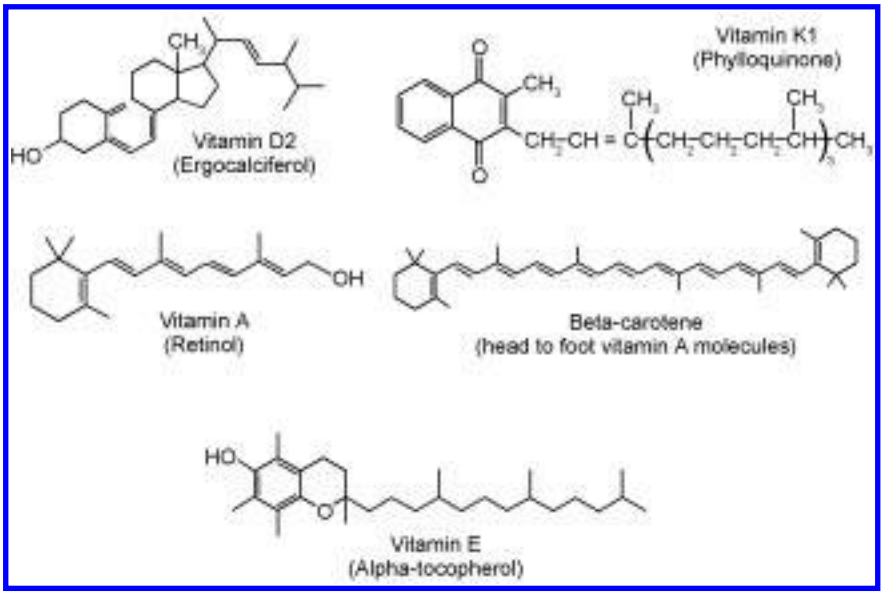

Fig. 19.1 Chemical structure of fat-soluble vitamins and provitamin molecules.

exposure. The main dietary sources of vitamin D are fatty fishes from cold sea: eel, salmon, mackerel and herring. Other dietary sources are mushrooms and dairy products. Fortified foods including milk/dairy products and cereals may also be important contributors to dietary vitamin D intake in many industrialized countries (Ovesen *et al.*, 2003). For the supply of vitamin D lack of foods containing vitamin D can be compensated by endogenous synthesis from the action of sunlight on the skin. During exposure to sunlight there is a conversion of 7-dehydrocholesterol to previtamin D3, rapidly isomerized into vitamin D3 under body temperature. Vitamin D3 is then excreted into the blood bound to vitamin D-binding protein. A first metabolic step in the liver (hydroxylation) leads to the formation of 25-hydroxyvitamin D and next, a second metabolic step in the kidney leads to the active metabolite of vitamin D, i.e. 1,25-dihydroxyvitamin D (calcitriol). As the level of calcitriol is correlated with that of 25-hydroxyvitamin D, the latter is also used to define vitamin D status. Renal calcitriol synthesis is regulated by parathyroid hormone (PTH) mostly to maintain body calcium level by increasing dietary calcium absorption and/or bone calcium resorption. In the cells calcitriol interacts with its vitamin D receptor (VDR).

Severe vitamin D deficiency leads to two main clinical signs: rickets and osteomalacia. Based on the latter, it can be said that vitamin D is intimately involved in bone mineralization. Indeed, vitamin D synthesis is controlled by calcium (inhibitor) and also by parathyroid hormone (stimulator) and in turn is actively involved in to calcium absorption from the gut. A main effect of 1,25(OH)2D is to increase the absorption of calcium from the gut. A poor

dietary calcium intake may increase calcium resorption from the bone to compensate low vitamin D endogenous synthesis. This can be related to observations that less severe deficiency has been associated with bone resorption, osteoporosis and fractures. Osteoporosis is defined as a progressive systemic skeletal disease with low bone mass and micro architectural deterioration of bone tissue and consequently an increase in bone fragility and susceptibility to fracture (WHO, 1994). Using knockout mice models (Panda *et al.*, 2004), it was suggested that the vitamin D receptor together with vitamin D are necessary for calcium absorption and bone growth. For the elderly, a relatively high intake of calcium (1500 mg/d) should be accompanied with an adequate level of vitamin D to absorb dietary (or supplemental) calcium (Utiger, 1998) efficiently, and to prevent or to decrease the rate of bone loss (Rodriguez-Martinez and Garcia-Cohen, 2002).

The term vitamin D refers to a group of steroid hormones super family of nuclear receptors, requiring metabolic activation as to act via its metabolites, mainly 1,25 dihydroxy-vitamin D [25(OH)D)]. These metabolites are bound to nuclear VDR that can modulate the transcription of vitamin D-dependent genes such as osteocalcine or calcium binding protein. Vitamin D receptors have been identified in numerous cell types and therefore vitamin D/VDR complex regulates the transcription of a number of genes depending on vitamin D response elements. Development and function of T cells, an important component of the body immune system, depend on vitamin D and vitamin D is thus linked to autoimmune diseases (Adorini, 2002). Similarly, expression of VDR in muscles suggested that vitamin D plays an important role in muscle function (Demay, 2003). In a longitudinal study, it was shown that individuals with vitamin D concentration lower than 25 nmol/L had a higher risk of developing sarcopenia (Visser *et al.*, 2003), a loss of muscle strength and mass usually associated with ageing (Roubenoff and Hughes, 2000).

Epidemiologic studies also revealed that cancer and vascular disease pathology risks are associated with vitamin D insufficiency. Vitamin D implication in cardiovascular disease and cancers has been revealed by an ecologic approach. Both in the USA and in European countries, significant relations were found between solar irradiance and reduction of breast, ovarian or colon cancer risk (Grant, 2006). For the latter, it was found that a serum level higher than 33 ng/mL has been associated with a 50% lower incidence of colorectal cancer (Gorham *et al.*, 2005). The link between cardiovascular diseases and vitamin D is rather indirect. Evidence comes mainly from studies in patients suffering from renal disease, associated with hyperparathyroidism who also show a higher risk from cardiovascular mortality (Foley *et al.*, 1998). In agreement with that, excess PTH has been associated with increased cardiovascular death and coronary heart disease (Sambrook *et al.*, 2004; Kamycheva *et al.*, 2004). Besides the inverse relationship between PTH and vitamin D levels, a comparison of European countries revealed that death from ischemic heart diseases increased with latitudes (Zittermann *et al.*, 2005). Recent experiments further established a more direct implication of vitamin D on cardiac function. Indeed, treatment with

vitamin D showed a cardio-protective effect either by a regression of myocardial hypertrophy in patients on hemodialysis (Kim *et al.*, 2006) or by reducing the inflammatory status of patients with congestive heart failure (Schleitoff *et al.*, 2006).

Even though no controlled intervention studies have yet been done to establish a causal relationship between low status of vitamin D and age-related degenerative pathologies, the above-mentioned epidemiological observations are strong enough to suggest that the elderly may need more 25(OH)D than younger adults (Vieth *et al.*, 2003). Indeed, in the elderly, it has long been recognized that serum concentrations of vitamin D are lower than those in the young. In surveys among institutionalized elderly people a prevalence reaching 75% is commonly found (Holick, 2003). Besides a decreased intake of vitamin D, such low status may also emerge from lower sunshine exposure and a reduced capacity of the aged skin to synthesize it. A low plasma Vitamin D level has always been associated with a high PTH level. Yet, normalization of vitamin D level by adequate dietary supply and/or vitamin D supplements may not result in normalization of plasma PTH because other factors including dietary calcium and renal function (glomerular filtration rate) regulate its level. In the elderly, both factors can be compromised and therefore contribute to a lower vitamin D status. Altogether the question is how best to maintain an adequate level of circulating vitamin D. Vitamin D required by the elderly has been determined by US and French national committees at 10–15 μg/d (IOM, 1997; Garabédian, 2001). Foods actually rich in vitamin D, such as eels or pike (24–25 μg/100g) are not as commonly used as eggs (2.8 μg/100g) or butter (0.3 μg/100g), which are rather poor dietary sources of vitamin D.

In six European countries, the estimated intake of vitamin D varied between 2.3 and 7.1 μg/d. These levels are far from the recommendations. In the same study, it was established that plasma vitamin D varied from 13–29 ng/mL during the winter time (Ovesen *et al.*, 2003). Similar or even lower values have been described in other elderly population studies (McKenna, 1992). However, there is no consensus on the optimal level of vitamin D, a value above which there is no further improvement of the outcome measured. For the latter, circulating PTH level has been chosen because of its implication in biological processes controlling bone mass. Indeed, in healthy subjects, vitamin D is by far the main regulator of serum PTH (Pepe *et al.*, 2004). Studies from Thomas *et al.* (1998) showed that the lowest plateau level of PTH is attained for a plasma level of 30 ng/mL or more of 25-hydroxyvitamin D. Interestingly, recent observations indicate that individuals having plasma level less than 32 ng/mL can be at risk of osteoporosis (Hollis, 2005). Therefore, higher plasma levels of vitamin D, i.e. 25-hydroxyvitamin D, e.g. over 40 ng/mLhave been proposed, acknowledging that values above 100 ng/mL are considered as toxic and may result in hypercalcemia/hypercalciuria. Clearly, determination of optimal level of circulating vitamin D level should be based on other biological parameters including parathyroid hormone (PTH) and calcium status. As already shown, vitamin D has been related with other health outcomes than bone disease. A recent meta-

analysis of double-blind randomized controlled trials looked into a variety of skeletal and non skeletal outcomes, including lower-extremity function, falls, dental health, and colorectal cancer (Bischoff-Ferrari *et al.*, 2006). In line with other published data (Gorham *et al.*, 2005), the review from Bischoff-Ferrari *et al.* suggests that a serum concentration of 30 ng/mL can be advantageous whereas the best effect was observed for a level of 36–40 ng/mL. To achieve such a level, present recommendations are largely insufficient, particularly for the elderly. The authors proposed an intake of 40 μg/d of vitamin D precursor (cholecalciferol) to bring vitamin D up to 30 ng/mL in no less than 50% of the population. Since most of the studies show a rather low vitamin D status, even in summer, it can be proposed that, in addition with rather usual low dietary intake (<10 μg/d), a supplementation of 15–20 μg/d might be necessary and safe for the subjects above 75 years old (Vieth, 1999, Tangpricha *et al.*, 2004).

19.3 Vitamin K

Vitamin K exclusively provided by the diet exists in two chemical forms, plant phylloquinone (vitamin K1) and menaquinones (vitamin K2 synthesized by bacteria). Both vitamins K are co-factors in the conversion of protein-bound glutamate residues to γ-carboxyglutamate residues. The latter conversion is necessary for the functionality of proteins such as anticoagulants involved in haemostasis, osteocalcin involved in bone calcification, and also of structural proteins of the cell matrix of most of tissues.

In most countries vitamin K intake is mainly as phylloquinones from plant foods (Bolton-Smith *et al.*, 2000; Booth *et al.*, 1993; Koivu *et al.*, 1997). Dark-green leafy vegetables and herbs are the most rich (kale, parsley, spinach, green cabbage; 300–600 μg/100g) followed by non leafy and pale leaves plants (white cabbage, lettuce, broccoli; 100–200 μg/100g). Globally, the values given in food composition table do not always take the variability inherent in plant foods into account, including maturity stage or losses during storage or processes. Altogether vegetables, most of them easily available, contribute to more than half of total vitamin K intake.

Interestingly, a small-scale study on fresh spinach, broccoli and lettuce, established that phylloquinone absorption was similar across plant species (Gijsbers *et al.*, 1996). As for many fat-soluble vitamins, phylloquinone is transported in triglyceride-rich lipoproteins. Intestinal absorption depends on the amount of energy from dietary fat. Indeed, bioavailability of vitamin K1 from spinach depends on its preparation with fat, which strongly improved the intestinal absorption (Gijsbers *et al.*, 1996). At dietary fat contents of 25 or 45% energy, no significant differences were observed in the absorption of vitamin K1 from spinach, broccoli and romaine lettuce (Garber *et al.*, 1999). Other studies also demonstrated that phylloquinone absorption from phylloquinone fortified oil ($\approx$400 μg/d) is greater than that from broccoli (Booth *et al.*, 2002), phylloquinone tablets (500 μg) and from spinach (Garber *et al.*, 1999). After

supplementation, plasma phylloquinone level decreased within nine hours to its baseline level.

The current recommendation is mainly based on normal clotting function as a primary criterion. The current RDA for vitamin K1 is 1 μg/kg body weight, and is in the range of average intake from foods. However, depletion studies with less than about 10 μg/d of phylloquinone for three weeks (Udall, 1965) or for 12 days (Ferland *et al.*, 1993) failed to affect the prothrombin time, a marker of hypoprothrombinemia, significantly despite a dramatic decrease of plasma phylloquinone level. Therefore, next to the older studies on haemostasis, recent ones mainly focus on the impact of vitamin K status on bone health. The use of vitamin K antagonists and phylloquinone-dependent undercarboxylation of osteocalcin were both associated with low mineral bone density and increased risk of fracture (Szulc *et al.*, 1993; Caraballo *et al.*, 1999). Recent epidemiological studies indicate that individuals with vitamin K intakes in the lowest quintiles are at risk of hip fracture (Feskanish *et al.*, 1999). The functional changes resulting from carboxylation of osteocalcin lead to consider the use of undercarboxylated osteocalcin as a sensitive marker of vitamin K status (Sokoll and Sadowski, 1996).

A recent study also proposed that the percentage of undercarboxylated osteocalcin may be a specific bone marker in early postmenopausal healthy women (Lukacs *et al.*, 2006). Controlled metabolic studies clearly indicated that resting plasma phylloquinone decreased rapidly after depletion and rose much more slowly after repletion (Ferland *et al.*, 1993; Booth *et al.*, 2003). Recent studies also show an inverse association between plasma phylloquinone and the percentage of undercarboxylated osteocalcin (Binkley *et al.*, 2000; McKeown *et al.*, 2002). Presently, there are indications that levels of intake as indicated above, may not be sufficient to completely maintain bone health. Vitamin K status determined from undercarboxylated osteocalcin showed a lower percentage of that protein after subjects consumed five times the current RDA (Booth *et al.*, 1999). Work from the same team also established that for each percentage decrease of undercarboxylated osteocalcin, there was an increase of 0.0008 g/cm^2 in bone mineral density (Booth *et al.*, 2004). Although small in magnitude, the contribution of vitamin K to carboxylate osteocalcin may be important to predict hip fracture risk in postmenopausal women (Cummings *et al.*, 1993). Indeed, elevated undercarboxylated osteocalcin has been associated with increased hip fracture risk; however, the relationship between carboxylated osteocalcin, a presumed active form, and bone health is not clear, since the level of this protein was found higher in hip fracture group (Vergnaud *et al.*, 1997).

Age-related differences in vitamin K status have been reported (Tsugawa *et al.*, 2006). However, during controlled vitamin K1 dietary restriction, elderly subjects show higher resistance to the development of subclinical signs (Ferland *et al.*, 1993). In post-menopausal women, it was noticed that vitamin K provides significant protective effect on bone health in those not taking estrogen (Feskanich *et al.*, 1999). In agreement herewith, is a recent study from Booth *et al.* (2004) which showed that among post-menopausal women not using

estrogen, low plasma phylloquinone status was associated with low spine bone density. Interestingly, serum undercarboxylated osteocalcin was negatively correlated with estradiol concentration (Yasui *et al.*, 2006).

Elderly healthy subjects also have significantly higher baseline plasma phylloquinone than younger subjects (Sadowski *et al.*, 1989; Binkley *et al.*, 2000). However, none of these studies reported values standardized for plasma lipids which are known to be increased in elderly individuals. On the other hand, bioavailability studies show differences between young and old individuals. A small-scale study from Booth *et al.* (1999) concluded that relative bioavailability of phylloquinone ($\approx$400 μg/d) from either a broccoli-rich diet or fortified oil did not differ between young (20–40) and elderly (60–80) subjects, even though the plasma level of phylloquinone after intake of fortified foods tends to be significantly higher in older subjects. Similar findings were found after individuals given vitamin K supplements at 1000 μg/d for 14 days (Binkley *et al.*, 2000). Whether such a high intake level is necessary for the elderly is still awaiting investigation. If activated osteocalcin level is necessary for the prevention of bone fracture, circulating vitamin K in oldest subjects should be kept higher than in younger ones. However, from epidemiological studies and from studies on the bioavailability of phylloquinone, it is suggested that there are no specific recommendations for the elderly group with adequate intake of vegetables and without specific treatment with drugs interfering with vitamin K metabolism. The present adequate intake for vitamin K, as settled by the American Committeee (Dietary Reference Intake, 2001), of 90 μg/day of vitamin K can be considered valid as well for young adults as for the elderly.

19.4 Vitamin A/provitamin A carotenoids

The term vitamin A refers to a family of molecules containing different functional groups in a cyclohexenyl group, and includes retinol, retinal, retinoic acid and retinyl ester. Dietary sources of vitamin A are mainly retinyl esters provided by animal-derived foods. In contrast with this pre-formed vitamin A, plant-foods bring vitamin A as provitamin A carotenoids such as β-carotene, α-carotene and β-cryptoxanthin. The carotenes are almost ubiquitously distributed in red to orange fruits and vegetables whereas β-cryptoxanthin is more specifically found in citrus fruits. Note that besides their pro-vitamin A property, specific actions have been attributed to these carotenoids (Krinsky and Johnson, 2005). Dietary retinyl esters were absorbed as retinol after hydrolysis of ester moiety, whereas, provitamin A carotenoids provide one (α-carotene and β-cryptoxanthin) or two molecules of retinol (β-carotene) when they are cleaved centrally. The cleavage is realized by beta-carotene monooxygenase (Yeum *et al.*, 2000). Retinol is then re-esterified by intestinal cells and transported into the liver by remnant chylomicrons via lymph.

Once in the liver, retinol binds to retinol-binding protein (RBP) and is transported from the liver to tissues as the *holo*-RBP complex. Serum retinol

concentrations are not associated with hepatic vitamin A over a wide range of liver values because *holo*-RBP is under homeostatic control (Underwood *et al.*, 1979). Vitamin A is stored into liver cells, and depending on body needs, it is re-oriented into tissues tightly bound on protein complex formed by retinol-binding protein and transthyretin. Plasma retinol is controlled so that plasma values below 1.05 μM clearly reflect vitamin A deficiency and levels above that value was considered as normal (Underwood, 1984). Note that such low plasma level was attained a relatively long time after effective decrease of vitamin A intake. The liver plays a major role in the homeostatic control of plasma retinol concentration, because it is the main storage organ for vitamin A in humans (Raica *et al.*, 1972). Vitamin A status as determined in the plasma depends on hepatic stores and the latter determination is a predictive biomarker of body vitamin A status. Two indirect methods can be used to assess hepatic stores namely the relative dose response test (RDR) and deuterated-retinol-dilution test (DRD). The RDR test consists of an oral load of vitamin A and assesses plasma changes before and after loading (Loerch *et al.*, 1979). If liver vitamin A storage is normal then additional vitamin A from oral charge will be stored into the liver and plasma retinol concentration will not change. If liver stores are low, newly absorbed vitamin A will be mobilized and the post oral-loading plasma concentration will increase. DRD technique (Baush and Rietz, 1977) consists on administration of labeled retinyl ester, determination of isotopic ratios in serum after the isotope has equilibrated with the body's vitamin A pool, and calculating total body stores (mainly liver store) with a mathematical formula developed by Furr *et al.* (1989).

Concerning the pro-vitamin A carotenoids, a number of factors affect bioavailability of carotenoids (Castenmiller and West, 1998). In particular, carotenoids dissolved into oils are better absorbed than the ones embedded into plant food matrix. To determine their respective contribution to vitamin A status, it was therefore necessary to develop equivalency between preformed vitamin A and provitamin A carotenoids. The latest proposal (Dietary Reference Intake, 2001) is based on Retinol Activity Equivalent (RAE). 1 μg RAE = 1 μg of all-*trans*-retinol = 2 μg of supplemental all-*trans*-β-carotene = 12 μg of dietary all-*trans*-β-carotene = 24 μg of other provitamin A carotenoids.

A high intake level of preformed vitamin A may lead to hypervitaminosis whereas no such an effect has been described for high intake of carotenoids. Fundamental studies indeed indicate that retinoic acid may inhibit the carotenoid-monooxygenase avoiding further cleavage of absorbed carotenoids (Bachmann *et al.*, 2002). Epidemiological observations indicated that beta-carotene intake in western countries is around 6 mg/d. Even though its contribution to vitamin A status seems rather low, it is not encouraged to increase that level at least with synthetic supplemental molecules since the deleterious effects described in two independent studies with individuals at risk for lung cancer (ATBC, 1994; Omenn *et al.*, 1996)

Because of the relative high quantity of vitamin A in Western diets and its homeostatic control by liver, the prevalence of vitamin A deficiency is

extremely low in populations of industrialized areas. Moreover, human liver concentration of vitamin A is maintained throughout life when dietary vitamin A is sufficient (Underwood *et al.*, 1970; Mitchell *et al.*, 1973). However, in countries with poor intakes, vitamin A deficiency is a real public health problem, affecting particularly the vision of children. On the other hand, the physiological ageing process may directly or indirectly affect vitamin A status, independently of intakes. Age-related alterations of gastrointestinal tract functions, of the enterocyte functions particularly the activities of lecithin-retinol acyltransferase and acyl CoA-retinol acyltransferase (Helgerud *et al.*, 1983; Ong, 1993), and of hepatic functions are expected to greatly affect vitamin A absorption, metabolism and status in the elderly. Early studies found no effect of age on vitamin A levels over the range 66–96 years (Black *et al.*, 1988; Comstock *et al.*, 1987; Hallfrisch *et al.*, 1994). This finding can be explained by misclassification of individuals with altered immune function, since serum retinol was lower in subjects with elevated CRP concentrations (Stephensen and Gildengorin, 2000). Recent studies found either that the higher retinol concentration occurred in older individuals – e.g. in among 12 741 volunteers in the French SUVIMAX trial (Faure *et al.*, 2006) – or that individuals in the highest quintile of plasma retinol level were the oldest ones (Fletcher *et al.*, 2003). In the elderly, most data on vitamin A status/metabolism were obtained in the post-prandial state. The intestinal absorption of vitamin A was shown to be higher in elderly (Johnson *et al.*, 1992; Krasinski *et al.*, 1990) or not markedly modified in a small-scale human study (Borel *et al.*, 1998). Note that a higher absorption was suggested by a higher plasma retinyl ester response which can be due to lower chylomicron remnant clearance rather than to increased intestinal absorption (Krasinski *et al.*, 1990). Delayed clearance was shown to occur in hyperlipemic subjects (Cohen and Grundy, 1992) and in normolipemic apolipoprotein E2 carriers (Weintraub *et al.*, 1987). On the other hand, little was known on the efficiency of vitamin A metabolism in the elderly, particularly on the processes involved in the mobilization of the liver vitamin A pool.

The essentiality of vitamin A is coming from the involvement of its oxidized metabolites (retinaldehyde and retinoic acids), in vision processes and cell/tissue growth and differentiation (Saari, 1994; Petkovitch *et al.*, 1987). Metabolites and synthetic compounds derived from vitamin A are now used as pharmacological compounds to cure diseases affecting the skin (Ott *et al.*, 1996; Sorg *et al.*, 2006) and cancers (Niles, 2000). A complex mechanism underlies the therapeutic effects of retinoic acid and its synthetic derivatives, involved in many pathophysiological events including normalization of cell differentiation and anti-inflammatory activities, both occurring in hyperproliferative and inflammatory diseases, such as acne, psoriasis, photoageing and neoplasias. Retinoids and their derivatives exert their action by activating transcription factors belonging to the superfamily of ligand-dependent nuclear transcription factors, the retinoic acid receptor (RAR) and retinoid X receptor (RXR) subfamilies of nuclear receptors. Once bound to nuclear factors, they are able to regulate gene expression in target cells (Nagpal

and Chandraratna, 1998). A great number of genes is co-regulated with other receptors that transduce hormonal signals from the immediate environment. As an example, retinoid X receptors (RXR) form heterodimers with the vitamin D receptor (VDR) or peroxisome proliferator-activated receptors (PPAR) transactivate expression of hormone response elements containing genes (Ebert *et al.*, 2006; Touzy and Schiffrin, 2006). Among age related diseases, recent studies focused on retinoid receptors as therapeutic targets for Alzheimer's disease (Goodman, 2006).

Ageing is a complex process in which immune status and function may play a pivotal role. Many studies undertaken in animal laboratories provided sound evidence that maintenance of both humoral antibody responses and cell-mediated immunity required vitamin A (Ross, 1996). Despite an association between low plasma vitamin A concentration and impaired immune function, no intervention studies have yet confirmed that vitamin A is directly involved in such immune system impairment in humans. Recent studies show, however, that ageing affects the retinoic acid receptors in healthy human peripheral blood mononuclear cells. The relative amount of mRNA of the retinoid acid receptor was significantly decreased in the elderly as compared with young subjects (Brtko *et al.*, 2007; Feart *et al.*, 2005). The physiological significance of such a finding remains to be investigated.

The relation between vitamin A and osteoporosis is a matter of debate. An ecological study indicated that hip fracture incidence was associated with a median intake of vitamin A up to six-fold higher in northern European countries than in southern Europe. Further, the work done by Melhus *et al.* (1998) showed that dietary intake of retinol greater than 1.5 mg/d was indeed associated with reduced bone mineral density and increased risk for hip fracture in Swedish individuals. Also, according to animal studies, it was assumed that a high level of vitamin A intake and a high serum retinol and/or retinyl esters level can be associated with a higher risk of osteoporosis (Michaelson *et al.*, 2003; Jackson and Sheehan, 2005; Penniston *et al.*, 2006).

The potential deleterious effect of intake levels near 1400 μg vitamin A/day on bone health strongly suggest to limit intake within the recommended dietary allowance of 700 and 900 μg/d for women and men, respectively. This can be particularly true for subjects of >60 y, since they may have an even lower tolerance for excessive retinol intake. Note that in the studies establishing an association between vitamin A and bone fracture, no relation was seen between either β-carotene intake (Feskanich *et al.*, 2002) or serum β-carotene level (Michaelsson *et al.*, 2003). These observations confirmed that carotenoids do not cause hypervitaminosis A even when ingested in large amounts. Interestingly, a recent study even demonstrated that beta-cryptoxanthin, a provitamin A carotenoid, has a preventive effect on ovariectomized-induced bone loss in vivo (Uchiyama and Yamaguchi, 2006).

19.5 Vitamin E

Vitamin E actually includes two groups of molecularly similar fat-soluble compounds, tocopherols and tocotrienols. They both contain phenolic moieties and are of plant origin. Alpha-tocopherol (α-Toc) is mainly found in sunflower seeds, olive oil and almonds; whereas most other oils and seed oils are rich in gamma-tocopherol (γ-Toc). Palm oil contains high amounts of tocotrienols. Besides plant oils, fruits and vegetables represent the second best dietary source of vitamin E. Thus, a balanced diet brings about 15–18 mg vitamin E per day and the recommendation is 12 mg/d for young adults and 20–50 mg/d for elderly (Cynober *et al.*, 2001).

Tocopherol compounds differ for their functional groups (hydrogen or methylene) found on the benzenyl ring of the common chromanol structure, and for their conjugated double bonds found in tocotrienols. The most widely distributed vitamin E molecules in mammalian tissues are represented by alpha-tocopherol (α-Toc). In humans, plasma level of α-Toc is about 28 μmol/L and values under 10–14 μmol/L are usually considered as indicative of deficiency. In a study with highly selected healthy volunteers from three European countries (Winklhofer-Roob *et al.*, 2003), it was found that plasma α-Toc significantly increased with age but not when standardized for cholesterol. Therefore in healthy individuals, it can be assumed that vitamin E status did not vary with age, as shown in the same study by looking at vitamin E levels in buccal mucosa cells. Introduced by Evans and Bishop (1922), this micronutrient was described as an essential dietary factor for reproduction in rats. The most efficient tocopherol component as fertility agent was found in the following order, α-Toc, beta-tocopherol (β-Toc), and gamma-tocopherol (γ-Toc). Interest in tocopherols and tocotrienols has been rapidly focused on their antioxidant properties. Indeed both the phenolic head and phytyl tails chemically contribute to their activity as chain-breaking antioxidants (Burton and Ingold, 1989). Their level and location as lipid-soluble components in cell membranes also leads to them being considered as the most important lipophilic radical-chain breaking antioxidant in tissues *in vivo*. The resulting oxidation product, i.e. tocopheroxyl radicals, may be regenerated, at least *in vitro*, by vitamin C located in the aqueous phase or by coenzyme Q located in cell and mitochondrial membranes, leading the concept of antioxidant recycling (Bascetta *et al.*, 1983). Recycling ascorbate through glutathione peroxidase extended the concept of antioxidant network. Within this network, vitamin E has been considered as central and, therefore, many studies focused on its use to prevent age-related pathologies and ageing by itself. Indeed, in all cases the resulting physiopathologic changes also induced oxidative stress. A controlled study with healthy volunteers clearly showed that dietary vitamin depletion for only three weeks, leads to a significantly higher *ex-vivo* LDL oxidizability, a marker of oxidative stress (Winklhofer-Roob *et al.*, 2003). However, *in vivo* studies (Tucker and Townsend, 2005) on cardiovascular disease, cancer, Alzheimer's disease led to skepticism regarding whether such interactions took place for maintenance of membrane tocopherols. More studies

had then been conducted on bioavailability, distribution and functions of tocopherols.

The distribution of vitamin E in the body depends on many proteins which act more or less specifically towards the different compounds of tocopherol's family. As all tocopherols are fat-soluble compounds, their absorption occurs at the proximal level of the small intestine and the compounds then join the circulation via lymphatic pathways assembled with other lipid constituents of chylomicrons. In the liver, α-Toc is specifically recognized by alpha-tocopherol transfer protein (α-TTP) and incorporated into VLDL particles. Then exchanges occur between the circulating lipoparticles, so that 90% of total serum α-Toc are 'transported' by LDL and HDL particles. It can be already said that the presence of α-TTP is the primary determinant of plasma and tissues level of vitamin E even if this protein also has relatively lower affinities for β-Toc and γ-Toc (Hosomi *et al.*, 1997). Vitamin E deficiency found in α-TTP knock-out mice was also associated with increased lesions in lipid peroxidation and lesions in the aorta (Terasawa *et al.*, 2000), demonstrating the role of vitamin E in cardiovascular risk.

Cellular uptake of α-Toc can occur through mechanisms already described for lipid transfer from lipoproteins and between cells. These include facilitated uptake by phospholipids transfer protein (PLTP) or lipoprotein lipase (endothelium, skeletal muscle, adipose tissue), LDL-receptor mediated endocytosis (ubiquitous), and more selective uptake by scavenger receptor class B type I also named SR-B1 (Mardones and Rigotti, 2004) in liver and steroidegenic tissues. It was shown that mice lacking PLTP have higher plasma α-Toc associated with LDL particles (Jiang *et al.*, 2002) whereas those lacking SR-B1 have also higher plasma α-Toc but associated with HDL particles (Mardones *et al.*, 2002). Interestingly, SR-B1 protein was shown to be over expressed in the liver of rats fed α-Toc free diet, partially reversed by control diet (Witt *et al.*, 2000). Deficiencies and/or dysfunction of these proteins may impair α-Toc distribution and may increase atherosclerotic risk. In particular, impaired distribution between plasma lipoproteins and tissues may increase plasma level of α-Toc with a concomitant decrease of α-Toc in the tissues.

Within the cell, α-Toc binding proteins have been described such as the α-Toc-associated proteins (TAP), ubiquitously expressed with preferential localization in liver, brain and prostate. It was proposed that TAP may transport α-Toc from plasma membranes to intracellular bilayers-delimited compartments (Zimmer *et al.*, 2000). Other proteins may be involved in the efflux of tocopherols from the cells. These proteins are known to secrete phospholipids and cholesterol into bile such as MDR2 and ABC-A1 (Mustacich *et al.*, 1998; Oram *et al.*, 2001).

Involvement of oxidized LDL as one of the first events in atherogenesis, and LDL being a main 'transporter' of vitamin E resulted into multiple intervention studies to prevent or retard cardiovascular disease using tocopherols as supplements (see Pryor *et al.*, 2000). Large and randomized clinical trials have not shown significant beneficial effect of use of vitamin E to reduce

atherosclerotic risk. In a recent retrospective review of literature, Robinson *et al.* (2006) proposed the following factors to explain the failure of clinical trials:

1. the inclusion of patients without biochemical evidence of increased oxidative stress,
2. the relatively short duration of treatment,
3. the use of suboptimal dosages of vitamin E,
4. the suppression of gamma-tocopherol by alpha-tocopherol,
5. the use of vitamin E supplementation without the concurrent use of vitamin C,
6. the lack of inclusion of biochemical markers of oxidative stress and markers of vascular response,
7. the inappropriate administration of vitamins relative to meal ingestion, and
8. the poor patient compliance and the lack of monitoring of vitamin E levels.

Note that in another recent meta-analysis from Wright *et al.* (2006), it was shown that higher plasma concentration of α-Toc within the normal range are associated with significantly lower total mortality and for oxidative pathologies including cardiovascular disease and cancer.

Interpretation of studies using vitamin E supplements has often been based on antioxidant properties of that vitamin and analogs. The antioxidant function against the deleterious effects of reactive oxygen and nitrogen species, is supposed to protect ageing and age-related chronic diseases including atherosclerosis, cancers, rheumatoid arthritis, Alzheimer's and Parkinson's diseases. However, studies first undertaken by Azzi's group clearly show that vitamin exerts cellular effects and that eventual beneficial effects could be due not to its antioxidant properties but rather on functions related to cell signaling and the resulting genes and protein expression (Azzi *et al.*, 2002). Thus, it was shown that the ability of α-Toc to inhibit smooth muscle cell proliferation cannot be reproduced by β-Toc, whereas both have similar free-radical scavenging activities. Non-antioxidant activities of vitamin E occurred at post-translational level by specifically activating (protein phosphatase 2A, diacyglycerol kinase) or inhibiting (protein kinase C, 5-lipoxygenase, phospholipase A2) the enzymatic activity (Zingg and Azzi, 2004). Non-antioxidant properties of vitamin E have also been related with regulation of several genes involved in the metabolism of α-Toc, the lipid uptake, the cell structure, the cell adhesion, and cell cycle (Azzi *et al.*, 2004).

Through its antioxidant property, vitamin E may act by modulating the intracellular redox status, a major determinant of transcription factor activation such as the nuclear factor kappa B (NF-κB) that controls the expression of spectrum different genes involved in inflammatory and proliferative responses (Rimbach *et al.*, 2002). Then, it can be said that vitamin E also modulates the expression and function of many proteins that are implicated in the above mentioned diseases. Therefore, the essential nutriment vitamin E status should be maintained at optimal level, 1 to 2 molecules of vitamin E per 2000–3000 cell membrane phospholipids, to avoid unbalanced situations where particularly a

high level may result in pro-oxidant activity of vitamin E and also may disturb the cell signaling role of that vitamin.

All these data accumulated for antioxidant and non-antioxidant actions of vitamin E demonstrate a central role of that vitamin for controlling many cell processes by either the protection of their structure against oxidative stress and/or the expression of many targeted age-related disease genes. On the other hand, vitamin E is a low toxicity compound (Morinobu *et al.*, 2002). Used at a level of 50 mg/d it is able to induce significant improvement of platelet aggregation and decrease of LDL oxidizability (Mabile *et al.*, 1999). Therefore, French experts advise to increase the daily intake of vitamin E from 20 to 50 mg, even though such a level can only be obtained with vitamin E as supplements whose beneficial or deleterious effects should be regularly followed (Cynober *et al.*, 2001).

19.6 Conclusions

The greatest difficulty in positioning the role of fat-soluble vitamins in the processes related to ageing by itself and in the associated pathologies is the complexity linked, on the one hand, to biological/physio-pathological ageing processes and, on the other hand, on the diet which is a sum of nutrients and not one particular compound. Ageing is a multifactorial process and the two main theories of ageing are based respectively on genomics and free radicals respectively. In the present work, the genomic aspect has not been developed even though it is largely known that ageing and the resulting longevity is related to heredity, which explains in most cases the large variation in human intervention studies. From laboratory studies, it can also be said that individuals exposed to oxidative stress are for sure at risk of lower longevity even when some individuals within the group may have genes to help them to live longer. Such an observation may be considered as an indirect way to imply free radicals, at the origin of oxidative stress, as potential actor for increasing the risk to develop pathologies. Similarly, it is also easy to provoke pathologies only using dietary means. For example, an unbalanced diet lacking vitamin C always lead to occurrence of scurvy. Health status has been positively increased in Western countries so that people from these countries live longer. In parallel, during ageing more age-related pathologies also appeared in those populations. Epidemiological observations indicate that there was a profound modification of the diet accompanying the Westernization. In particular an increased intake of refined and fatty products was found together with a decreased intake of plant-based foods. Such an observation also leads to hypothesize that micronutrients which are indeed found at lower level in such diets, may contribute to morbidity and mortality in those populations. Many studies were then undertaken to precisely define these micronutrients and their potential role in the prevention. Among these, minerals and trace element, vitamins and carotenoids, and more recently polyphenols were re-visited as well scientifically as economically by

offering to the individuals some pills containing one or more of these micronutrients as dietary supplements. From the studies described above on fat-soluble vitamins, it can be said that the rationale for using supplements is far from clear today.

From the development on data given above for each fat-soluble vitamin, it can also be seen that all were implied in one or more processes related to either ageing and/or age-related diseases. This means that there is a limit for extending all these data into application in everyday life. Indeed, diet provides all of these vitamins and carotenoids, sometimes at once. It is sometimes difficult and more often impossible to extend a mechanism of action of one compound when this is incorporated into a complex diet. More studies are needed to look for the action and the mechanisms underlying these actions when interactions occur between the fat-soluble vitamins and the other macro- and micro-nutrients in the foods. In the fat-soluble vitamins area alone, it was already shown that vitamin A and vitamin D influence the synthesis of several vitamin K-dependent proteins (Fraser *et al.*, 1988; Cancela and Price, 1992) or that a high vitamin E-induced hemorrhagic syndrome can be counteracted by vitamin K administration (Rao and Manson, 1975). Modern studies, using 'omics' technologies, i.e. genomic, proteomic or metabolomic approaches, are thus necessary to further determine the impact of interactions of micronutrients at cellular and molecular level and the consequences on biological/physiological functions. Other perspectives lay on better understanding the link between dietary intake and functions of fat soluble vitamins which are controlled by protein machinery such as vitamin A and vitamin E and those known to interact with nuclear receptors (vitamin A and vitamin D) or to modulate effects on transcription factors (vitamin E). Such a link may then provide scientific sound evidence on an 'optimal' level of vitamins that should be ingested daily.

19.7 Sources of further information and advice

Many websites referred to vitamins and nutrition of ageing. Very often, most of the key words used lead to commercial sites and links. Attempts were made to inform the consumers about the benefits for vitamins but as these also have commercial aims, there is a need for scientific background to better understand and to critically evaluate this information. For the latter purpose, there are reviews such as the one given above and others referenced in the database Pubmed from US National Library of Medicine (*www.ncbi.nlm.nih.gov/entrez/*). there are also other handbooks developing specific areas on nutrition and ageing (*Handbook of Nutrition in the Aged*, 3rd edition. Ed Ronald R. Watson, CRC Press, Boca Raton, 2001) and on vitamins (*Handbook of Vitamins*, Ed R.B. Rucker, J.W. Suttie, D.B. McCormick, L.J. Machlin, Marcel Dekker, Inc. New York, Basel, 2001). To precisely define the fat-soluble vitamin needs of elderly, a series of books have been edited by US Institute of Medicine (Dietary Reference Intakes, Institute of Medicine, National Academy Press, Washington,

D.C. 2001). Note that the values given in those books may differ according to European countries. Therefore, one can also refer to other national publications for comparing with other sources including those from the United States.

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20

Water-soluble vitamins and ageing

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Abstract: Since their discovery, the importance of the water-soluble B complex vitamins and vitamin C to the maintenance of healthy tissue and prevention of disease has been recognized. Today, research on the actions of these vitamins is leading to the understanding that these vitamins function in complex ways in the body to maintain optimal health, and to protect against chronic diseases of ageing, including cardiovascular disease, cognitive decline and osteoporosis. The present chapter presents an updated summary of these advances in understanding of function, along with information on their dietary sources and bioavailability.

Key words: vitamin C, thiamin, riboflavin, niacin, folate, vitamin B_6, vitamin B_{12}.

20.1 Introduction

Since their discovery in the early part of the 20th century, the importance of the water-soluble B complex vitamins and vitamin C to the maintenance of healthy tissue and prevention of disease has been recognized. Deficiency of these vitamins led to severe consequences. Beriberi was a condition common among impoverished populations consuming polished rice. This progressive disease led to peripheral neuropathy, progressive leg paralysis and, in some cases (wet beriberi), edema and congestive heart failure. After noting the association of this condition with polished rice, investigation led to the discovery of thiamin – a substance in the outer husk, but not in the polished grain of the rice – as the necessary factor for prevention of this disease. Pellagra, resulting in the 4-Ds – diarrhea, dementia, dermatitis and death – was a devastating condition in the early-20th-century southern United States among sharecroppers depending on corn as a staple. Although originally thought to be caused by a toxin in corn, the

lack of niacin or vitamin B_3 was eventually identified as the causal factor. Similarly, scurvy, with deterioration of skin and membranes, was common on long sailing voyages. It was first found to be cured by use of citrus fruit, and the substance responsible, vitamin C, was discovered later. These dramatic examples of the human requirement for specific vitamins launched the field of nutrition and demonstrated the importance of a varied and high quality diet.

Fortunately, the discovery of the vitamins allowed for widespread effective intervention to prevent these devastating deficiencies in most parts of the world today. However, inadequate intake of these and the other members of the B complex family persist. Today, research on the actions of these vitamins is leading to the understanding that beyond the prevention of deficiency diseases, these vitamins function in complex ways in the body to maintain optimal health, and to protect against chronic disease. This is particularly important for the growing ageing population, where changes in energy requirement, and decline in metabolic efficiency make it difficult to ensure adequate vitamin intake. Recent advances in understanding the roles of individual vitamins demonstrate the power of several of these, particularly the B vitamins, in the prevention of most chronic diseases of ageing, including cardiovascular disease, cognitive decline and osteoporosis. With the exception of vitamin B_{12}, which is stored in the liver, these water-soluble vitamins are not stored and, therefore, regular intakes are needed. The present chapter presents an updated summary of these advances in understanding of function, along with information on their dietary sources and bioavailability. Although all the recognized B vitamins are noted below, the focus is on those which have recently been shown to have important associations with chronic conditions of ageing, and for which intakes in the older adult population are frequently inadequate. Chemical structures of these water-soluble vitamins are shown in Fig. 20.1, and features are summarized in Table 20.1.

20.2 B vitamin complex

The B vitamins include thiamin (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5) pyridoxine (B_6), biotin (B_7), folate (B_9), and vitamin B_{12}. Although during the discovery period others were identified and thought to be vitamins, they were later proven not to be essential substances, and thus dropped from this list. Most of the B vitamins work together as coenzymes, facilitating the myriad metabolic processes in the body. They are essential for the breakdown of macronutrients in the diet – carbohydrates, fat and protein – for energy production, and they participate in reactions that affect the integrity of cells. Disruptions in any of these metabolic systems have consequences that can range from the serious deficiencies noted above, to less obvious, but important effects on the health of the nervous system, the vascular system and the muscular-skeletal system. The nervous system, in particular, is sensitive to the adequacy of B vitamins and a growing body of recent research shows associations with mood and cognition in ageing populations, as well as with peripheral neuropathy

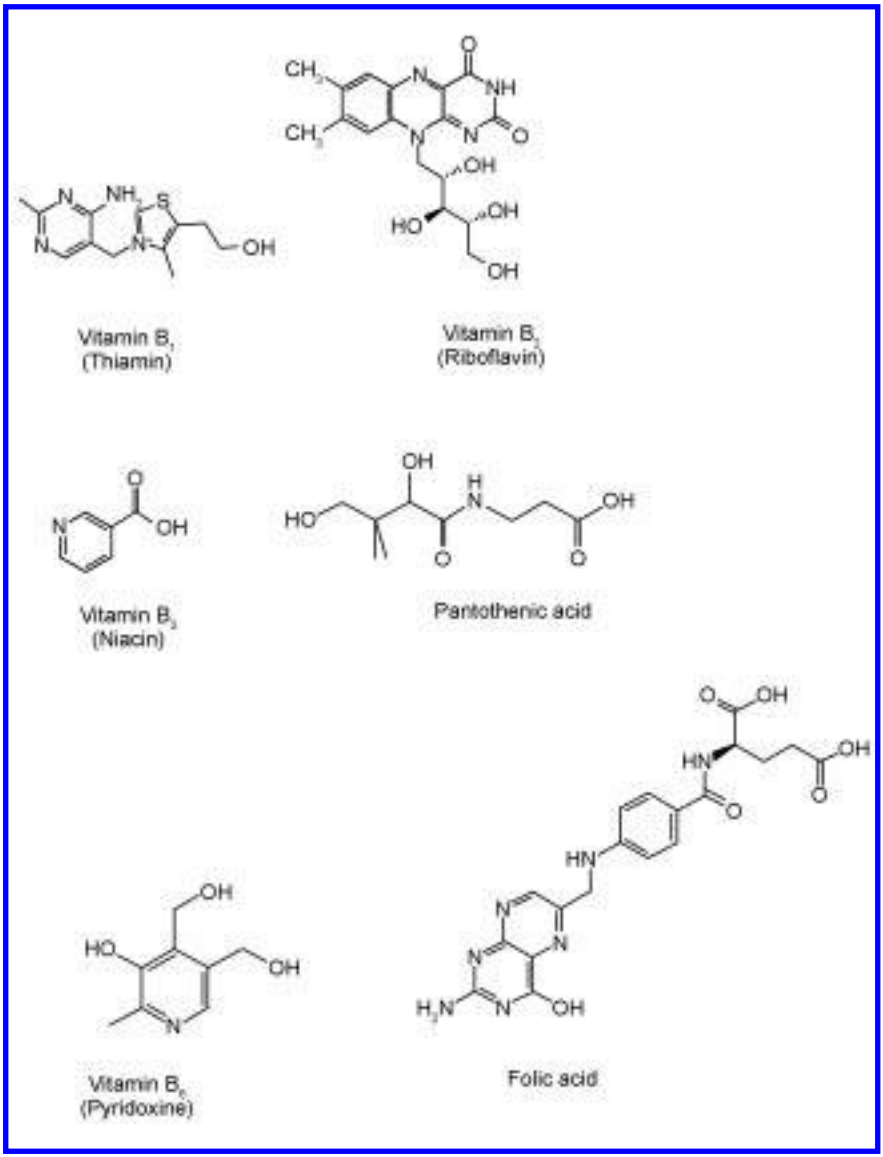

Fig. 20.1 Chemical structure of water-soluble vitamins.

and balance. Although supplementation with a single B vitamin has been shown to correct deficiencies associated with the particular vitamin, effects on chronic conditions appear less amenable to single nutrient intervention. These nutrients work closely together in many metabolic reactions, and it is, therefore, important to ensure adequacy of all, ideally with a high quality diet. Because this is often difficult for elderly individuals, a multiple vitamin-mineral supplement is often recommended. With the exception of vitamin B_{12}, as discussed below, the use of

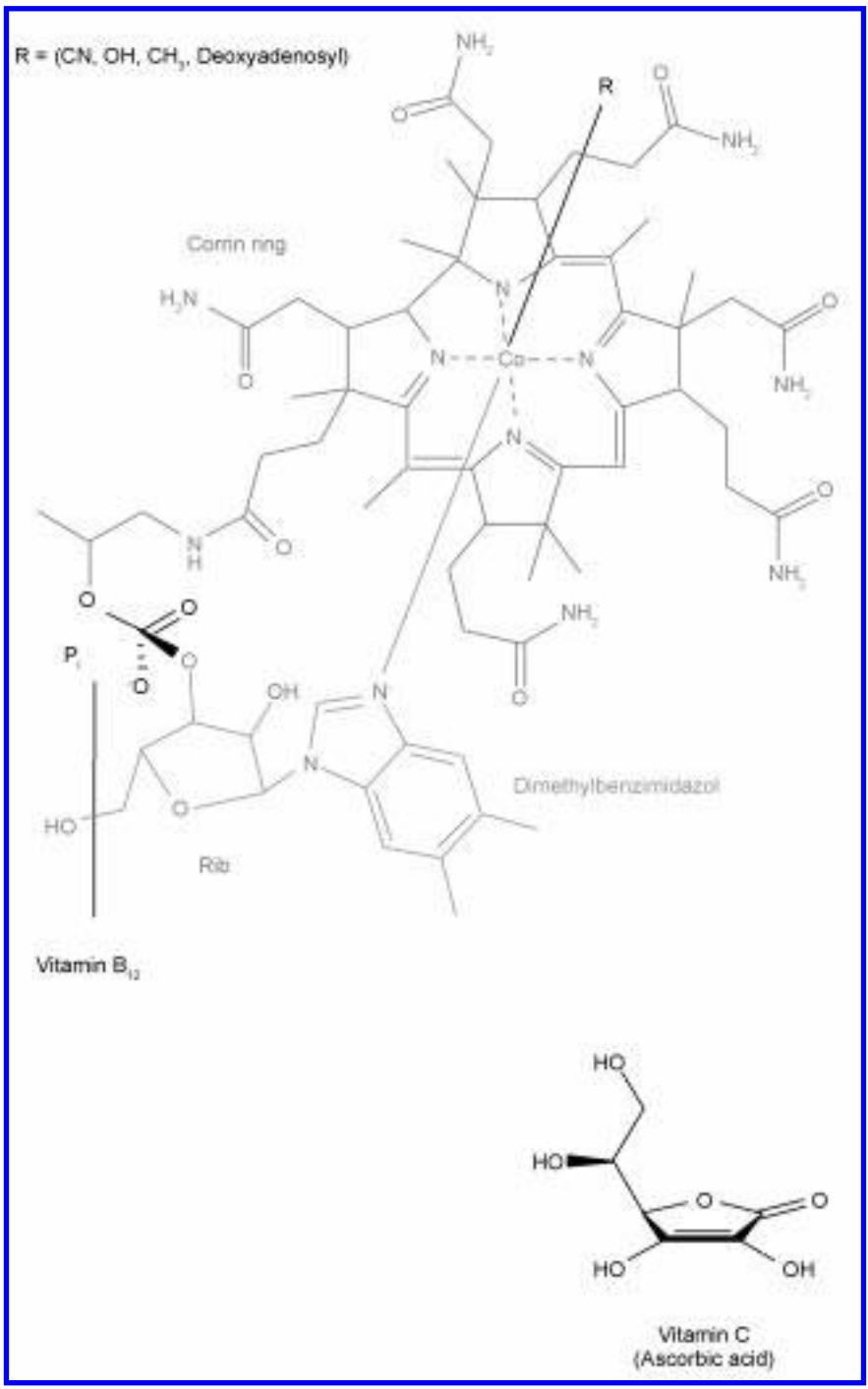

Fig. 20.1 Continued

Table 20.1 Water-soluble vitamins: sources and their importance for elderly individuals

Vitamin	Chemical name	Dietary sources	Particularity	Deficiency signs	Preventive effect	Normal plasma concentration	RDA*	
							Men	Women
Thiamin	Thiamin pyrophosphate (TPP)	Whole-grains, pork, legumes, nuts and seeds, enriched grain products	Decarboxylation of α-ketoacids and branched-chain keto acids Transketolation of hexose and pentose phosphates	Beriberi Wernicke-Korsakoff syndrome Weakness, gait disturbance, anorexia, weight loss, apathy, decrease in short-term memory, confusion, irritability, and muscle weakness	May improve mood	% transketolase stimulation by TPP > 20% indicates deficiency (index > 1.2)	1.2 mg/d	1.1 mg/d
Riboflavin		Milk, yogurt, cheese, lean beef, pork, liver, salmon, green leafy vegetables, legumes, eggs, nuts, seeds, whole-grains, enriched grain products	Glutathione reductase, an FAD-dependent enzyme, is important for protection against reactive oxygen species FMN, a strong oxidizing agent, is the major form in cells and tissues	Cheilosis (cracked lips) Angular stomatitis (cracks at the corners of the mouth) Inflamed red tongue Seborrheic dermatitis	May contribute to lower plasma homocysteine May reduce the risk of age-related cataract	% glutathione reductase stimulation by FAD > 40% indicates deficiency (index > 1.4)	1.3 mg/d	1.1 mg/d

Table 20.1 Water-soluble vitamins: sources and their importance for elderly individuals

Vitamin	Chemical name	Dietary sources	Particularity	Deficiency signs	Preventive effect	Normal plasma concentration	RDA*	
							Men	Women
Niacin	Nicotinic acid and nicotinamide: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP)	Legumes, nuts, lean meats, fish and whole-grain breads and cereals	Red blood cell production Synthesis of hormones and fatty acids	Pellagras: bilateral photosensitive rash on hands, feet, neckline and face; glossitis and stomatitis; abdominal distension, esophageal burning, constipation or diarrhea; dementia, psychosis, delirium Mild: weakness, lack of appetite, depression skin infections	Possible protection against cancer	24-hour urinary excretion of <5.8 μmol/day represent deficient niacin and 5.8 to 17.5 μmol/day represent low status	16 mg/d	14 mg/d
Pantothenic acid		Liver, whole grains, eggs, yogurt, avocado, broccoli	Synthesis of coenzyme A (CoA)	Experimental depletion has led to headache, insomnia, numbness and tingling of the hands and feet			5 mg/d†	5 mg/d†
Vitamin B_6	Pyridoxal 5′-phosphate (PLP)	Liver, fish, pork, chicken, avocados, nuts, beans, wheat germ, bananas	PLP-dependent enzyme is needed to synthesize neurotransmitters	Seborrheic dermatitis, glossitis, angular stomatosis, microcytic anemia, depression, confusion, neuropathy and convulsions	May be beneficial for cognitive function and mood	30 nmol/L has been used as the lower end of normal status but 20 nmol/L is also used	1.7 mg/d	1.5 mg/d
Biotin		Liver, egg, whole grain, avocado	May play a role in DNA replication and transcription	Hair loss, scaly rash on face and genital area; depression, hallucination; numbness and tingling of extremities	May be important in prevention of type 2 diabetes		30 μg/d	30 μg/d

Folate	Tetrahydrofolate (FH_4)	Liver, mushrooms, green leafy vegetables, dried beans, fortified grain products	Acts as a coenzyme in single-carbon transfers in metabolism of nucleic and amino acids; acts as a substrate in the conversion of homocysteine to methionine, for further conversion to *S*-adenosyl-methionine – for methylation reactions	Megaloblastic anemia Neural tube defects Depressed mood and mental function	Needed to prevent high homocysteine, which is associated with heart disease and cognitive decline Possible role in cancer prevention	Deficiency suggested at <5 ng/mL, however, 3 ng/mL is also used	400 μg/d	400 μg/d
Vitamin B_{12}	Cyanocobalamin Methylcobalamin	Found naturally almost exclusively in animal foods	Acts as a coenzyme in the pathway that converts homocysteine to methionine	Megaloblastic anemia Neurologic deterioration with symptoms of tingling and numbness in extremities, reduction in vibration and position sense, gait disturbance, memory loss, disorientation, insomnia, incontinence, visual disturbance and dementia	May be protective against heart disease, cognitive decline and Alzheimer's disease	Frequently used clinical cutoff point is < 185 pmol/L (250 pg/mL)	2.4 μg/d	2.4 μg/d
Vitamin C	Ascorbic acid	Fruit and vegetables: particularly citrus fruits, tomatoes, cruciferous vegetables, potatoes	Powerful water-soluble antioxidant	Scurvy: bleeding gums, impaired wound healing, follicular hyperkeratosis, perifollicular hemorrhages, ecchymoses, fatigue, depression and eventually hair and tooth loss, excessive bleeding and death	May be associated with lower risk of cardiovascular disease, non-hormone-dependent cancers, cataract	0.5–1.4 mg/dL (30–80 μmol/L)	90 μg/d	75 μg/d

*RDA for Life Stage Group $\geq$ 51 y
†Adequate Intake (AI)

single B vitamins is not generally recommended and may lead, in some cases, to imbalances that may exacerbate rather than contribute to prevention of some chronic conditions.

20.3 Vitamin B_1, thiamin

The first of the B vitamins discovered, thiamin remains an important vitamin in the public health of the ageing population. In its active coenzyme form, thiamin pyrophosphate (TPP), thiamin acts in the metabolism of carbohydrates and branched-chain amino acids. Important reactions involve the decarboxylation of α-ketoacids such as pyruvate, α-ketoglutarate, and branched-chain keto acids, and transketolation of hexose and pentose phosphates. Erythrocyte transketolase activity is used as a functional test of thiamin status. Erythrocytes are lysed and transketolase activity is measured before and after addition of TPP. The activity coefficient is defined as the post-addition level of transketolase activity, as a multiple of the basal level (McCormick and Greene, 1994). Marginal deficiency is defined when the activity coefficient is between 1.20 and 1.25, and deficiency when it is > 1.25 (Schrijver, 1991).

Although beriberi is now rare, inadequacies in thiamin intake continue to exist and to have less obvious but also important effects on human metabolism and chronic conditions. Deficiency continues to be seen primarily in chronic alcoholics, as a form of beriberi known as Wernicke-Korsakoff syndrome. High alcohol intakes increase thiamin requirement while, at the same time, alcoholics often have poor quality diets. Wernicke-Korsakoff syndrome affects the brain, with distortions in eye movement, gait and mental function including amnesia and confabulation. Less is known about the effects of subclinical deficiencies of thiamin in older individuals, but inadequacy is likely under-diagnosed as the symptoms tend to be non-specific in nature and include weakness, gait disturbance, anorexia, weight loss, apathy, decrease in short-term memory, confusion, irritability, and muscle weakness (Wilson, 1983).

The estimated average requirements (EARs) and recommended daily intakes (RDAs), respectively for thiamin for adults ages 50 and older are set at the same level as for younger adults – 1.0 and 1.2 mg/day for men and 0.9 and 1.1 mg/day for women (Food and Nutrition Board and Institute of Medicine, 1998). Natural food sources of thiamin include whole-grain products, pork, legumes, nuts and seeds. In the United States and most other countries, thiamin is added to enriched white flour, along with niacin, riboflavin and now folic acid. Major sources, therefore, include enriched bread and bread products, and fortified ready-to-eat cereals. Thiamin is heat sensitive and therefore vulnerable to food processing. Data from the recent NHANES (2003–04) for individuals aged 70 years and older show mean thiamin intakes of 1.6 for men and 1.3 for women. However, despite evidence of general intake adequacy relative to current recommendations, several studies suggest that a substantial percentage of the elderly population may have at least mild deficiency of thiamin. European

studies have shown low biochemical values for more than 20% of an elderly sample in Finland (Pekkarinen *et al.*, 1974), and 23% of a sample of Dutch older individuals (Hoorn *et al.*, 1975). A more recent study of 2379 elderly persons participating in the Elderly Nutrition and Health Survey in Taiwan (1999–2000) showed that 16.5% of men and 14% of women were thiamin deficient and another 14.7% of men and 11.9% of women were marginally deficient (Yang *et al.*, 2005). Many B vitamins, including thiamin, may be affected by medication use. A study of hospitalized elderly subjects, found that low thiamin plasma concentration was prevalent, and was associated with the use of diuretics (Suter *et al.*, 2000).

Owing to the appearance of adequate dietary intake in most populations, few studies have been conducted on the role of thiamin in chronic conditions. However, at least four studies have shown that thiamin supplementation improved mood in older individuals (Benton and Donohoe, 1999). More research is needed to better understand both the prevalence of low thiamin and its contribution to chronic disease.

20.4 Vitamin B_2, riboflavin

Like thiamin, riboflavin is important to energy metabolism. It is the central component of flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) and is required for a wide variety of cellular metabolic processes. Glutathione reductase, an FAD-dependent enzyme, is important for protection against reactive oxygen species (Powers, 1999). FAD can accept one or two electrons, and is reduced in the citric acid cycle to $FADH_2$ during aerobic respiration. These reduction potentials are used in the electron transport chain to generate ATP in the mitochondria, regenerating FAD. FMN is a strong oxidizing agent and is the major form of riboflavin in cells and tissues. Because these coenzymes are required for many metabolic reactions in the body, a deficiency in riboflavin can affect the status and function of several other nutrients, including vitamin B_6 and niacin (Madigan *et al.*, 1998; McCormick, 1999). Flavocoenzymes participate in niacin dependent dehydrogenations, and oxidative decarboxylations involving thiamin (McCormick and Greene, 1994). They are also involved in the formation of some vitamins and their coenzymes. For example, an FMN-dependent oxidase catalyzes the conversion of the 5′-phosphates of vitamin B_6 to coenzymic pyridoxal 5′-phosphate, and an FAD-dependent dehydrogenase reduces 5,10-methylene-tetrahydrofolate to the 5′-methyl product that interfaces with the B_{12}-dependent formation of methionine from homocysteine. Riboflavin has also been implicated in anemia, possibly though effects on iron absorption and utilization and the production of red blood cells (Madigan *et al.*, 1998). Riboflavin status is most commonly evaluated with erythrocyte glutathione reductase, a functional indicator, expressed as an activity coefficient (EGRAC) – the ratio of activities with and without added FAD (Sauberlich *et al.*, 1972). An EGRAC ratio of 1.0 indicates no stimulation,

suggesting that adequate amounts of FAD (riboflavin) were originally present. Although variations in standardization exist, EGRAC ratios of 1.2 to 1.4 are generally considered to be associated with moderate deficiency and those greater than 1.4 to indicate deficiency (McCormick and Greene, 1994).

Classic symptoms of riboflavin deficiency include cheilosis (cracked lips), angular stomatitis (cracks at the corners of the mouth) as well as inflamed red tongue and seborrheic dermatitis. These symptoms have been observed with inadequate dietary intake of riboflavin in developing countries, but overt clinical signs are currently rare. However, there is likely widespread subclinical riboflavin deficiency in the population, particularly among older adults.

The estimated average requirements (EARs) and recommended daily intakes (RDAs), respectively, for riboflavin for adults ages 50 and older are – 1.1 and 1.3 mg/day for men and 0.9 and 1.1 mg/day for women (Food and Nutrition Board and Institute of Medicine, 1998). Natural food sources include milk, yogurt, cheese, lean beef, pork, liver, salmon, green leafy vegetables, legumes, eggs, nuts and seeds, and whole-grain products. Although riboflavin is more heat stable than thiamin, it is degraded by light, so the use of light-blocking containers for major sources, such as milk, is important. Because dairy products are an important source of riboflavin, older individuals who do not include dairy products in their diet are more susceptible to deficiency than those who regularly consume milk and milk products. Mean intakes for US elders (aged 70 years and older) were reported as 2.3 mg for men and 1.8 mg for women in the NHANES 2003–04. However, despite the appearance of adequate mean intakes, riboflavin deficiency may be more common in older individuals than is generally appreciated. It is exacerbated by several chronic conditions, suggesting increased requirement in diabetes and heart disease (Food and Nutrition Board and Institute of Medicine, 1998). Estimates of deficiency vary greatly. The 1994–95 British Diet and Nutrition Survey found that, among those 65 years of age and older, 10% reported low dietary intake of riboflavin, but 41% had low status, based on biochemical assessment (Bates *et al.*, 1999). In the Elderly Nutrition and Health Survey in Taiwan, the prevalence of riboflavin deficiency was 7% for elderly males and 4% for elderly females, with marginal deficiency present in another 26% of males and 20% of females (Yang *et al.*, 2005). Very high prevalences of riboflavin deficiency have been reported in developing countries, where milk intake is low. In Guatemala, 50–76% of older adults were found to be deficient (Boisvert *et al.*, 1993).

Limited research has been conducted on the role of riboflavin in preventing chronic disease with ageing, but new studies show that it is emerging as an important nutrient. Although homocysteine has been primarily linked with folate and vitamins B_{12} and B_6, a recent study showed that higher plasma riboflavin concentrations were associated with lower plasma homocysteine in individuals homozygous for the C677T polymorphism of the methyl tetrahydrofolate reductase (MTHFR) gene, when folate intake was also low (Jacques *et al.*, 2002). There is also epidemiologic evidence to suggest that riboflavin intakes of greater than 1.6 to 2.2 mg/day may reduce the risk of developing age-related

cataracts (Cumming *et al.*, 2000; Jacques *et al.*, 2005). Although controversial, a few studies suggest a potential role for riboflavin in cancer prevention. Some, but not all, studies of low riboflavin intake and esophageal cancer have shown a significant protective effect (Powers, 2003). A recent study in Iran reported that individuals were twice as likely to develop esophageal cancer in riboflavin-deficient households than in non-deficient households, although an earlier study by the same authors did not find this association (Siassi *et al.*, 2000; Siassi.and Ghadirian, 2005).

20.5 Vitamin B_3, niacin

Niacin works together with other B vitamins in many aspects of cellular metabolism, including the release of energy from carbohydrates and processing of alcohol. It is mainly in two forms – nicotinic acid and nicotinamide – which are used in the body as the derivatives nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). These function as coenzymes in oxidation-reduction reactions. Levels of oxidized and reduced forms of these coenzymes regulate mitochondrial electron transport and numerous enzyme reactions. Important niacin dependent reactions include those associated with building red blood cells, and synthesizing hormones and fatty acids. Among other roles, NAD functions as a co-dehydrogenase with enzymes in the oxidation of energy related molecules, including lactate, alcohol, pyruvate, and α-ketoglutarate; while NADP functions in fatty acid and steroid syntheses. Niacin status is assessed by urinary excretion of N^1-methylnicotinamide (NMN) and its 2-pyridone derivative (N^1-methyl-2-pyridone-5-carboxamide). Using 24 hour urine samples, excretion rates of <5.8 μmol/day represent deficient niacin status and 5.8 to 17.5 μmol/day represent low status (Sauberlich *et al.*, 1974).

Fortunately, niacin deficiency and the clinical manifestations of pellagra are now rare, but deficiency does occur – often in association with alcoholism. Niacin deficiency can produce symptoms in skin, mucous membranes, the gastro-intestinal tract and the central nervous system. With pellagra, skin lesions appear as a photosensitive rash, usually bilaterally symmetric on exposed areas of the skin, including the hands, feet, neckline and face. Oral lesions include glossitis and stomatitis, with redness and pain. Abdominal distension and burning in the esophagus with either constipation or diarrhea have also been reported. Progression of deficiency leads to dementia and psychosis with memory impairment, disorientation and delirium. Milder symptoms may differ in different individuals, and this deficiency may, therefore, be difficult to distinguish between other B vitamin deficiencies. Mild symptoms may include muscular weakness, lack of appetite, skin infections, indigestion and depression.

Niacin differs from the other B vitamins in that it can be produced by the body if the amino acid tryptophan is available in sufficient supply. For this reason, the dietary requirement is expressed as niacin equivalents (NEs). Therefore, protein adequacy – particularly from dairy products, which are high

in tryptophan – protects against deficiency. Approximately 60 mg of tryptophan is required for synthesis of 1 mg of niacin, equal to 1 NE. The estimated average requirements (EARs) and recommended daily intakes (RDAs), respectively, for niacin for adults ages 50 and older are 12 and 16 NE/day for men and 11 and 14 NE/day for women (Food and Nutrition Board and Institute of Medicine, 1998). Because the niacin in corn is not available for absorption unless it is treated with lime, deficiency has been common where people use un-limed maize as a staple with simultaneous limitations in protein intake. Food sources of niacin include legumes, nuts, lean meats, fish and whole-grain breads and cereals. Niacin is also lost in milling of flour, along with thiamin and riboflavin, and like these other two vitamins, is added back to enriched flour. Most dietary surveys show intakes of NE well above requirements in the general population, but, as for thiamin and riboflavin, older adults with low energy and protein intake may not have sufficient niacin intake. Adults aged 70 and above in the recent NHANES reported mean niacin intakes of 22.6 mg for men and 18.5 mg for women. High levels of niacin can cause flushing and, based on this, a Tolerable Upper Intake Level (UL) for niacin for adults has been set at 35 mg/day.

Niacin has received relatively little attention in relation to chronic disease. Some interest in its possible protection against cancer is based on *in vitro* studies showing that NAD is consumed as a substrate in ADP-ribose transfer reactions, and that the activity of poly (ADP-ribose) polymerase, an enzyme activated by DNA strand breaks, can deplete NAD. Studies of DNA damage in cultured cells support the hypothesis that niacin may limit carcinogenic events (Jacobson, 1993). However, there is little evidence of an association between cancer and niacin in human populations. Significantly lower incidence of oral and esophageal cancers was associated with higher niacin intake in a case control study in Italy and Switzerland (Franceschi *et al.*, 2000; Negri *et al.*, 2000), but causal inference is not clear as several micronutrients were associated with reduced risk. One recent study showed a protective association between niacin intake and incident cognitive impairment and Alzheimer's disease, but this has not been confirmed in other studies (Morris *et al.*, 2004).

20.6 Pantothenic acid

Pantothenic acid is used in the synthesis of coenzyme A (CoA), an essential coenzyme for the transfer of carbon atoms in energy metabolism, and for the synthesis of many compounds, including acetylcholine, fatty acids, cholesterol, heme and steroid hormones. Because pantothenic acid is found in most foods, deficiency is extremely rare and has only been reported in situations of extreme deprivation. Experimental depletion has led to complaints of headache, insomnia, and numbness and tingling of the hands and feet which were reversed with administration of pantothenic acid (Hodges *et al.*, 1958). Similar symptoms have been seen in prisoners of war during World War II (Plesofsky-Vig, 1996). The US Food and Nutrition Board has not set an RDA for pantothenic acid, but

lists 5 mg/day as an adequate intake (AI) (Food and Nutrition Board and Institute of Medicine, 1998). Foods high in pantothenic acid include liver, whole grains, eggs, yogurt, avocado and broccoli. Because low intakes of pantothenic acid are rare, there have been few studies on its relation to health and disease.

20.7 Vitamin B_6, pyridoxine

While referred to as pyridoxine, vitamin B_6 appears in several related forms, including pyridoxine, pyridoxal and pyridoxamine. The active form in the body is as pyridoxal 5′-phosphate (PLP), which is known to have a role in the function of more than 100 enzymes. It is important for energy metabolism as in amino acid metabolism, in gluconeogenesis from amino acids, and as a coenzyme for glycogen phosphorylase, which catalyzes the reaction that releases glucose from glycogen. It is important for the brain, as a PLP-dependent enzyme is needed to synthesize neurotransmitters, including serotonin, dopamine, norepinephrine and gamma-aminobutyric acid. PLP also acts as a coenzyme in the synthesis of heme for red blood cells, assists the conversion of tryptophan to niacin, binds to steroid hormone receptors to modulate the effects of hormones like estrogen and testosterone, is involved in one-carbon metabolism, and in the synthesis of nucleic acids (Leklem, 1999; Mackey *et al.*, 2006). Plasma PLP is most commonly used to assess vitamin B_6 status. Its concentration has been shown to correlate with other indices of B_6 status. A plasma PLP concentration of 30 nmol/L has been suggested as the lower end of normal status (Leklem, 1990), but 20 nmol/L is also widely used.

Severe vitamin B_6 deficiency is currently rare, but occurs – as do other B vitamin deficiencies – most frequently in alcoholics. Symptoms overlap with those of riboflavin deficiency – seborrheic dermatitis, glossitis, angular stomatosis – but also include microcytic anemia, depression, confusion, neuropathy and convulsions (Leklem, 1999; Mackey *et al.*, 2006). Because of the central role that vitamin B_6 plays in numerous metabolic reactions, there is currently growing interest in the likelihood that subclinical deficiency of vitamin B_6 may contribute to chronic disease.

The estimated average requirements (EARs) and recommended daily intakes (RDAs), respectively for vitamin B_6 for adults ages 50 and older are – 1.4 and 1.7 mg/day for men and 1.3 and 1.5 mg/day for women (Food and Nutrition Board and Institute of Medicine, 1998). Vitamin B_6 is prevalent in a variety of whole foods. Good sources include liver, fish, pork, chicken, avocados, nuts, beans, wheat germ, and bananas. In the 2003–04 NHANES, the mean reported intakes of vitamin B_6 were 1.9 and 1.6 mg/d for men and women, respectively, aged 70 years and older. Dietary surveys consistently show that large proportions of older adults have intakes of vitamin B_6 that fall below the recommendations (Russell and Suter, 1993; Marshall *et al.*, 2001; Buell *et al.*, 2007; Kamphuis *et al.*, 2007), and that plasma PLP is often low in population-based surveys, particularly in older adults (Haller *et al.*, 1991; Russell and Suter,

1993). On the other hand, high intakes of vitamin B_6 have been associated with sensory neuropathy. Based on this, the Food and Nutrition Board set the tolerable upper intake level (UL) for vitamin B_6 at 100 mg/day for adults (Food and Nutrition Board and Institute of Medicine, 1998).

Suboptimal intakes and plasma status of vitamin B_6 have been associated with several chronic conditions and research is currently active in this area. Because high plasma homocysteine has been identified as a risk factor for heart disease, the vitamins involved in its metabolism have also been implicated. Homocysteine is an intermediate in the metabolism of methionine, and is catabolyzed through two main pathways involving B vitamins. In the transsulfuration pathway, homocysteine is converted to cysteine with the assistance of two PLP-dependent enzymes. When vitamin B6 is inadequate, the elevation in homocysteine seen with a methionine load (as occurs with a protein meal), is not cleared efficiently (Selhub *et al.*, 1993). One prospective observational study reported a 30 percent reduction in incidence of coronary heart disease (CHD) between individuals in the highest and lowest quintiles of vitamin B_6 intake (Rimm *et al.*, 1998). Several other studies have also shown associations between heart disease and vitamin B_6 (Robinson *et al.*, 1995; Folsom *et al.*, 1998; Robinson *et al.*, 1998; Lin *et al.*, 2006). Vitamin B_6 has also been associated with cognitive function in elderly populations. In the Veterans Administration Normative Ageing Study of men, vitamin B_6 status, evaluated by plasma PLP concentrations, was related to two out of a battery of about 20 cognitive tests (Riggs *et al.*, 1996). A more recent examination of the same cohort revealed significant declines in cognitive scores among those with the lowest tertile of plasma PLP as well as of dietary intake (Tucker *et al.*, 2005). Some, but not all B vitamin supplementation trials have shown beneficial effects on cognitive scores (Balk *et al.*, 2007), and more research is needed to confirm a protective effect of vitamin B_6. Because vitamin B_6 is important for neurotransmitter synthesis, it has also been hypothesized that relatively low vitamin B_6 status may be implicated in depression. In a population of Puerto Rican adults in Massachusetts, where depression is a prevalent problem, both vitamin B_6 intake and status (PLP) were associated with scores on the Center for Epidemiologic Studies Depression Scale (CES-D), suggesting a possible effect of vitamin B6 on this condition (Merete *et al.*, 2008). Again, more research is needed to clarify these associations. Low vitamin B_6 intake and status have also been associated with impaired immune function, especially in the elderly. Decreased production of lymphocytes and interleukin-2 has been reported in vitamin B_6 deficient individuals, while restoration of vitamin B_6 status has normalized lymphocyte proliferation and interleukin-2 production (Meydani *et al.*, 1991).

20.8 Vitamin B_7, biotin

Biotin is an important component of the enzymes acetyl-CoA carboxylase, which is required for the synthesis of fatty acids, pyruvate carboxylase, for

gluconeogenesis, methylcrotonyl-CoA carboxylase, for leucine metabolism, and propionyl-CoA carboxylase, for the metabolism of amino acids, cholesterol and odd chain fatty acids (Chapman-Smith and Cronan, 1999). Another enzyme, biotinidase, has been shown to catalyze the acetylation and methylation of histones, suggesting that biotin may play a role in DNA replication and transcription (Hymes and Wolf, 1999).

Deficiency of biotin is rare. Interestingly, deficiency has occurred with prolonged consumption of raw egg white, due to its content of the protein avidin which binds biotin and prevents its absorption. However, cooking denatures the avidin, and therefore, cooked eggs do not block the absorption of biotin. Deficiency symptoms include hair loss and a characteristic scaly red rash on the face and genital area. Depression, hallucination, and numbness and tingling of the extremities have also been reported in association with biotin deficiency (Mock, 1999). The Food and Nutrition Board did not have sufficient information to set an RDA for biotin, but did set an adequate intake level (AI) of 30 μg/day for adults (Food and Nutrition Board and Institute of Medicine, 1998). This amount should be met by most varied diets. Good sources include liver, egg, whole grains and avocado. Because deficiency is rare, few studies have been conducted on biotin and health in human populations. There is, however, some evidence that biotin may be important in the prevention of type 2 diabetes. Lower biotin concentrations have been noted in diabetes patients relative to controls and, further, biotin supplementation has been shown to reduce blood glucose concentrations in patients (Maebashi *et al.*, 1993). More research is needed to understand the implications of these observations.

20.9 Vitamin B_9, folate

Folate acts as a coenzyme in single-carbon transfers in the metabolism of nucleic and amino acids. In its natural state, folate occurs as several pteroyl-polyglutamates, which contain one to six additional glutamate molecules joined in a peptide linkage to the γ-carboxyl of glutamate. Although rarely found in food, folic acid (pteroylmonoglutamic acid) is the form used in supplements and fortified foods, as it is the most stable form. Folate coenzymes are required for deoxyribonucleic acid (DNA) synthesis and normal cell division, for purine synthesis, for generation and utilization of formate, and for interconversion of amino acids. The latter role includes the conversion of homocysteine to methionine, thereby preventing the accumulation of homocysteine while providing methionine for further conversion to *S*-adenosyl-methionine – which is needed for methylation reactions (Wagner, 1996). Folate metabolism is tightly linked with that of vitamin B_{12}, which is why deficiency of either results in megaloblastic anemia. The formation of 5,10-methylene tetrahydrofolate depends on the regeneration of tetrahydrofolate in the homocysteine-to-methionine conversion, with folate as a substrate (5-methyl-tetrahydrofolate) and vitamin B_{12} as a coenzyme. 5,10-methylenetetrahydrofolate delivers its

methyl group to deoxyuridylate to form thymidylate for incorporation into DNA. Because of its central role in DNA formation, folate deficiency has its greatest effects on rapidly dividing cells.

The most commonly used measures of folate status are serum or plasma folate. Although there has been concern that serum or plasma folate may fluctuate with recent intake, Jacques *et al.* showed that it correlated well with estimates of usual dietary intake (Jacques *et al.*, 1993). Erythrocyte folate is also used as a longer term measure. Deficiency has typically been considered at a serum folate concentration of less than 7 nmol/L (3 ng/mL) (Herbert, 1987). However, recent data relating serum or plasma folate to homocysteine concentration suggest that there is evidence of metabolic disturbance at higher concentrations (Jacques *et al.*, 1999). Thus, a cutoff point of 5 ng/mL is also frequently used.

Folate deficiency has been more common than most other B vitamin deficiencies. The major sign is megaloblastic anemia with enlarged red blood cells, and hypersegmented neutrophils. This anemia leads to fatigue, weakness, irritability, headache, palpitations, and shortness of breath (Lindenbaum *et al.*, 1988). This anemia may also be caused by vitamin B_{12} deficiency, so once megaloblastic anemia is identified, additional tests are necessary to determine cause. Low dietary intake is the primary cause of folate deficiency, and this may be aggravated by heavy alcohol use. Subclinical deficiency of folate is related to elevated homocysteine which, as discussed above, has been associated with risk of heart disease. The US food supply was recently fortified with folic acid, the supplemental form of the nutrient, based on the association between low folate intake in early pregnancy and incidence of neural tube defects.

The EAR and RDA for both men and women aged 50 years and above, are 320 and 400 μg/day of dietary folate equivalents (DFEs), respectively. This relatively new definition is used because the food supply now contains a mixture of natural folates in food, and folic acid, added as a fortificant. Folic acid is more bioavailable than that from food. Using the current definition, 1 μg DFE = 0.6 μg folic acid from fortified food or from a supplement taken with meals = 1 μg of food folate = 0.5 μg from a supplement taken on an empty stomach (Food and Nutrition Board and Institute of Medicine, 1998). Good natural sources of folate include green leafy vegetables, like spinach, oranges and orange juice, legumes and whole grains. In countries which have fortified refined grains with folic acid, these have also become major sources. In the recent NHANES 2003–04, mean DFE intakes for men and women aged 70 years and older were 533 and 452 μg, respectively. However, only 197 and 181 μg, respectively were from food folate, demonstrating the large effect that fortification of foods has had on US folate intakes. European countries are currently considering the addition of folic acid fortification to their food supply on a country to country basis. A German survey of adults 65 years and older revealed that 37% did not reach two-thirds of the recommended amount for folate intake (Volkert *et al.*, 2004).

While the fortification of the food supply has been considered a success in reducing neural tube defects, and in reducing folate deficiency, there are

concerns about the high levels of folate now in the US food supply, particularly for the ageing population. It has long been known that high intakes of folic acid will mask the hematological symptoms of an underlying vitamin B_{12} deficiency. Of greater concern is evidence that excess folic acid intake may precipitate or exacerbate the neurological damage of vitamin B_{12} deficiency. Case reports have demonstrated the onset or progression of neurological complications in vitamin B_{12}-deficient individuals receiving supplemental folate. In addition, vitamin B_{12}-deficient monkeys receiving supplemental folic acid were shown to develop signs of neuropathology earlier than control monkeys (Agamanolis *et al.*, 1976). Because vitamin B_{12} deficiency is relatively common in the elderly population, and because progression can lead to irreversible nerve damage if not identified and treated, these concerns are important. Taking this risk into account, the Food and Nutrition Board set the upper limit for folate at 1000 μg/day from fortified food or supplements. Evidence from national surveys suggest that for some individuals, consumption of fortified breakfast cereals and cereal grains along with a multivitamin supplement can easily exceed this UL. Further research is needed to clarify the risks and benefits of this exposure.

In the ageing population, folate has received considerable attention in relation to risk of heart disease and cognitive decline, given its central role in prevention of elevated homocysteine. A 1997 meta-analysis of 20 studies estimated that each increment of 5 mmol/L of total homocysteine was associated with a 60% greater risk of CHD for men and 50% greater risk for women (Beresford and Boushey, 1997). Similar risks were identified for cerebrovascular disease and peripheral vascular disease. Mechanisms suggested for these effects include the possibilities that homocysteine exerts a direct toxic effect on endothelial cells, promoting atherosclerotic lesions (Tsai *et al.*, 1994) and that it increases adhesiveness of platelets, increasing clotting (Harpel *et al.*, 1996). Alternatively, a more direct effect of folate, by restoring or preserving endothelium function and integrity by affecting cellular oxidative metabolism, has also been proposed (Verhaar *et al.*, 1998).

Several studies have linked folate with depressed mood and mental function (Reynolds *et al.*, 1973; Goodwin *et al.*, 1983). In a study of normally ageing men in Boston, elevated homocysteine, low plasma folate and low dietary intake were each significantly associated with cognitive decline over three years (Tucker *et al.*, 2005). The effect of low folate on brain function is likely to be through its role in one-carbon metabolism (Alpert and Fava, 1997). Methylene tetrahydrofolate is important in maintaining adequate methionine for synthesis of *S*-adenosylmethionine (SAM), a key cofactor in neurotransmitter synthesis and metabolism in the brain (Turner, 1977). It has also been hypothesized that folate dependent methylation reactions may be important for maintaining neuronal and glial membrane lipids (Hirata *et al.*, 1980).

Another active area of folate research is its possible role in cancer prevention. It is thought that poor folate status may enhance an underlying predisposition to cancer (Mason and Levesque, 1996). One study found that individuals with human papilloma virus-16 (HPV-16) infection had a five-fold greater risk of

cervical dysplasia if they had low erythrocyte folate values (Butterworth *et al.*, 1992). Potential mechanisms for a cancer promoting effect of low folate include DNA hypomethylation, increased chromosomal fragility or diminished DNA repair (Kim *et al.*, 1997). Low folate has also been associated with colorectal cancer. Two large prospective studies support the inverse association between folate intake and incidence of colorectal adenomatous polyps and cancers (Giovannucci *et al.*, 1993; 1995). Those in the highest quintile of folate intake (approximately 800 μg/day) had a relative risk of 0.65 for adenoma, relative to those in the lowest quintile of folate intake (approximately 200 μg/day). The combination of low folate and high alcohol increased the risk significantly. Glynn and colleagues also observed a significant four-fold increase in risk of colorectal cancer in subjects with high alcohol and low folate intakes (Glynn *et al.*, 1996).

20.10 Vitamin B_{12}

Vitamin B_{12} functions as a coenzyme (methylcobalamin) in the pathway that converts homocysteine to methionine which, in turn, is required for the synthesis of S-adenosylmethonine, a methyl donor needed for DNA methylation. Vitamin B_{12} is also used as 5-deoxyadenosylcobalamin, for conversion of L-methylmalonyl-coenzyme A (CoA) to succinyl-CoA. This reaction is important for the production of energy from fats and proteins and for the synthesis of hemoglobin. Inadequate vitamin B_{12} will, therefore, lead to elevations in both circulating homocysteine (which may also be elevated due to folate deficiency) and methylmalonic acid (which is specific to vitamin B_{12}).

Vitamin B_{12} deficiency has widely been known as 'pernicious anemia,' arising from a lack of intrinsic factor due to severe gastric atrophy. Intrinsic factor is produced by parietal cells of the gastric mucosa, and is required for vitamin B_{12} to be absorbed by the small intestine. Pernicious anemia is generally caused by an autoimmune response that destroys the parietal cells. In addition, antibodies to intrinsic factor bind to intrinsic factor, preventing it from binding to vitamin B_{12}. However, vitamin B_{12} deficiency may also be caused by low vitamin B_{12} intake, by atrophic gastritis, which leads to inflammation of the gastric lining and decreased acid production, or by medications that reduce stomach acid, notably H_2 receptor antagonists and proton pump inhibitors. Stomach acid is necessary to denature (unfold) proteins, so that they can be broken down and the vitamin B_{12}, which is bound to protein in foods, released.

The prevalence of vitamin B_{12} deficiency is significant among older adults (Tucker *et al.*, 2000; Clarke *et al.*, 2004; Flood *et al.*, 2006; Hin *et al.*, 2006). The anemia that results from vitamin B_{12} deficiency is a megaloblastic anemia that is indistinguishable from that which occurs with folate deficiency, characterized by macrocytosis and elevated mean cell volume along with pallor and fatigue. Additional indicators may include hypersegmentation of polymorphonuclear leukocytes, neutropenia and thrombocytopenia (Carmel *et al.*,

1996). Vitamin B_{12} deficiency can also lead to serious neurological problems, with progression to irreversible damage if not treated. Early neurological symptoms include tingling and numbness in the hands and feet, and reductions in vibration and position sense. Additional symptoms vary, but include gait disturbance, memory loss, disorientation, insomnia, incontinence, visual disturbance and dementia. As detection of vitamin B_{12} deficiency has traditionally depended on follow-up after diagnosis of megaloblastic anemia, there is concern that the addition of folic acid to the food supply, as was recently implemented in the United States, may 'mask' the deficiency, leading to neurological progression. It has been increasingly noted that vitamin B_{12} deficiency may present without anemia, suggesting that dependence of this indicator is not reliable for detection. Further, there is accumulating evidence that the combination of high folate and low vitamin B_{12} may accelerate the progression of neurological damage from the vitamin B_{12} deficiency. Some studies have noted that vitamin B_{12} deficient patients without anemia showed more severe neurological complications than those with megaloblastic anemia (Healton *et al.*, 1991; Savage *et al.*, 1994a). The hematologic symptoms are reversible with treatment, but evidence suggests that the neurological complications are reversible only if treated relatively soon (generally within one year) after their first appearance (Bethell and Sturgis, 1948; Healton *et al.*, 1991). It is, therefore, of considerable importance to detect any deficiency at an early stage.

The EAR and RDA for vitamin B_{12} for men over the age of 50 years are 2.0 and 2.4 μg/d, respectively (Food and Nutrition Board and Institute of Medicine, 1998). These have been based on the avoidance of megaloblastic anemia and on the maintenance of serum vitamin B_{12} concentrations. This assumes that 50% of the vitamin B_{12} ingested is absorbed. However, owing to decline in stomach acid with age, up to 30% of older people may be unable to absorb naturally occurring vitamin B_{12} in foods (Krasinski *et al.*, 1986). In vitamin supplements and in fortified foods, like breakfast cereals, vitamin B_{12} is in crystalline form, and is more readily absorbed when stomach acid is low, as it does not need to be separated from protein. In a study of absorption of radio-labeled B_{12} in older adults (49–69 y), all of the patients with low vitamin B_{12} concentrations (<125 pmol/L) and elevated serum gastrin showed very low absorption (less than 12%) of food-bound B_{12} compared with 21% of those with low vitamin B_{12} but normal serum gastrin values, and with none of the patients with serum B_{12} concentrations above 125 pmol/L (170 pg/mL). The latter group absorbed 12–39% of food-bound vitamin B_{12} and 54–97% of crystalline vitamin B_{12} (Miller *et al.*, 1992). For this reason, the most recent recommendations note that 'it is advisable for those older than 50 years to meet their RDA mainly by consuming foods fortified with vitamin B_{12} or a vitamin B_{12}-containing supplement' (Food and Nutrition Board and Institute of Medicine, 1998). However, it should be noted that the RDA is set for healthy individuals. For many older adults with absorption problems and existing deficiency, much higher intakes may be needed. A recent dosing study (Eussen *et al.*, 2005) found that between 650 and 1000 μg per day were needed to correct mild vitamin B_{12} deficiency in elderly

participants within 24 weeks. These amounts are prescribed commonly for vitamin B_{12} deficiency, and appear to be safe, with no evidence of detrimental side effects. Mean daily dietary intakes of vitamin B_{12} for men and women aged 70 years and older in the recent NHANES 2003–04, were 6.1 and 4.1 μg/day, respectively. Although absorption is the primary cause of vitamin B_{12} deficiency in older adults, low intake is also a concern for many, and intake has been shown to correlate with plasma concentrations (Tucker *et al.*, 2000).

Vitamin B_{12} deficiency is typically measured by serum or plasma concentrations. Although these reflect both dietary exposure and stores, existing cutoff points have relatively poor sensitivity and specificity. A frequently used clinical cutoff point is 185 pmol/L (250 pg/mL). However, individuals with clinical evidence of deficiency have been documented at higher concentrations, suggesting that the use of this cutoff point would miss cases (Lindenbaum *et al.*, 1988). It is therefore recommended by some that a higher clinical cutoff point be used to identify possible deficiency, followed by the measurement of methylmalonic acid, as a functional metabolic indicator of vitamin B_{12} deficiency. Because patients with vitamin B12 deficiency have been identified with serum or plasma vitamin B_{12} concentrations as high as 250 pmol/L (350 pg/mL), this cutoff point has been used in the literature (Savage *et al.*, 1994b; Holleland *et al.*, 1999; Refsum *et al.*, 2004). As noted above, when vitamin B_{12} is inadequate, methylmalonic acid (MMA) will not be efficiently cleared and concentrations will be elevated. However, although considered a more sensitive indicator of vitamin B_{12} deficiency than serum or plasma vitamin B_{12} concentration, MMA may also be elevated due to kidney disease or to bacterial overgrowth in the intestinal tract (Lindenbaum *et al.*, 1990). As measurements vary, precise cutoff values for MMA remain unclear, but the range for expected variability has been noted as 73–271 nmol/L (Pennypacker *et al.*, 1992). New tests for holo-transcobalamin II (Holo-TC II) are also used to determine the amount of vitamin B_{12} that is directly available to cells, but this test remains experimental. Tests for serum gastrin and pepsinogen are used to help diagnose pernicious anemia – low stomach acid stimulates gastrin production elevating levels, while low levels of pepsinogen I relative to pepsinogen II are seen in pernicious anemia.

Vitamin B_{12} is found naturally almost exclusively in animal foods. Average intakes tend to be well above the RDA in the United States and most Westernized countries. Exceptions include strict vegetarians and vegans and others restricting animal food intake. The elderly are also at risk of low intake when total energy intakes and animal food intakes are reduced with anorexia or food insufficiency. This compounds the problem of poor absorption and use of medications which may interfere with absorption in this age group.

Because low vitamin B_{12} will lead to elevated homocysteine, it has been associated with heart disease, cognitive decline and Alzheimer's disease (Clarke *et al.*, 2007). In addition, vitamin B_{12} deficiency has been linked with depression due to the importance of methylation reactions to the synthesis of neurotransmitters (Tiemeier *et al.*, 2002). These are currently active areas of research.

20.11 Vitamin C

Most animals, guinea pigs and humans being exceptions, can synthesize ascorbic acid. Humans lack the enzyme L-gulonolactorne oxidae and therefore cannot synthesize this nutrient, making ascorbic acid a vitamin required from the diet. Vitamin C functions primarily as a powerful water-soluble antioxidant. Because it has high reducing capability, it is able to quench reactive oxygen and nitrogen species. Ascorbate provides antioxidant protection throughout the body and has been shown to protect the eye against photo-generated free-radical damage (Delamere, 1996), the semen, against oxidative damage to sperm DNA (Fraga *et al.*, 1991), and the cardiovascular system – by protecting against lipid peroxidation (Frei *et al.*, 1988). Vitamin C is an electron donor for enzymes important to collagen hydroxylation, and to hormone and amino acid synthesis, including those important to the synthesis of the catecholamines norepinephrine and epinephrine. In addition to collagen synthesis, there is evidence that vitamin C is important to other components of connective tissue, including elastin, fibronectin, and bone matrix (Ronchetti *et al.*, 1996). Vitamin C has also been shown to be important to the larger antioxidant system, by regenerating α-tocopherol and glutathione to their active states (Jacob, 1995).

The classic vitamin C deficiency is scurvy, where collagen has broken down leading to loss of integrity of membranes throughout the body. This results in multiple symptoms, including bleeding gums, impaired wound healing, follicular hyperkeratosis, perifollicular hemorrhages, ecchymoses, fatigue, depression and eventually hair and tooth loss, excessive bleeding and death (Levine *et al.*, 1996). Scurvy was common on long sailing voyages when sailors went without fresh fruit or vegetables for long periods of time, and before vitamin C was discovered, it was recognized that citrus fruit would cure scurvy. Today scurvy is rare, but occurs occasionally in alcoholics or others with severe dietary restriction. However, the optimal dose of vitamin C has been controversial, as it has been promoted for a variety of health conditions including avoidance of the common cold, heart disease, cancer and cataract.

The estimated average requirements (EARs) and recommended daily intakes (RDAs), respectively for vitamin C for adults ages 50 and older are – 75 and 90 mg/day for men and 60 and 75 mg/day for women. These numbers are based on antioxidant protection, as assessed by maintenance of maximal neutophil ascorbate concentration, with little urinary ascorbate excretion (Food and Nutrition Board and Institute of Medicine, 2000). Smoking increases oxidative stress and, thus, the utilization of vitamin C and it is therefore recommended that smokers have higher intakes. Others have suggested that these RDAs are too low, and promote much higher intakes of vitamin C. For example, Nobel laureate Linus Pauling was famous for recommending more than 1000 mg/day to reduce the incidence of the common cold (Pauling, 1976). Subsequent clinical trials did not generally support this claim, but they did suggest some benefit in reducing the severity of the cold with vitamin C supplementation – but without the need for such high doses (Anderson, 1975). A recent meta-analysis of 29

trials noted reduction of cold duration by 8% with administration of 200 mg/d (Douglas *et al.*, 2004). The Linus Pauling Institute currently recommends that older adults have 400 mg/day of vitamin C, based on a recent study showing that plasma vitamin C became fully saturated at 400 mg/day in young women participating in a depletion repletion study (Levine *et al.*, 2001). While the authors of that study concluded that the RDA for young women should be raised to 90 mg/day, the Linus Pauling Institute argues that older adults should consume at least 400 mg/day to protect against chronic disease, and because of lower cellular uptake with ageing (Higdon, n.d.). This remains controversial.

Mean daily intakes of vitamin C for men and women aged 70 years and older in the recent NHANES 2003–04, were 85 and 83 mg, respectively (NHANES 2003–04). Vitamin C is generally nontoxic, but a tolerable upper intake level (UL) for adults was set at 2 g/day by the US Food and Nutrition Board, based on osmotic diarrhea and gastrointestinal disturbances (Food and Nutrition Board and Institute of Medicine, 2000). Most vitamin C in the diet comes from fruit and vegetables – particularly from citrus fruits, tomatoes, cruciferous vegetables and potatoes (Sinha *et al.*, 1993). Being water-soluble, vitamin C is easily lost in cooking water during boiling. It is also destroyed by heating to temperatures greater than 190 ºC, which may be reached with pressure cooking, roasting, frying and grilling food.

Considerable research has been conducted on the role of vitamin C on chronic disease risk. Prospective cohort studies have shown that relatively higher vitamin C intakes were associated with lower risk of cardiovascular disease (Knekt *et al.*, 1994). A British study of 730 elderly men and women (Gale *et al.*, 1995) found that vitamin C intakes greater than 45 mg/day were associated with a 50 percent lower risk of stroke than were intakes less than 28 mg/day. The antioxidant activity of vitamin C has been shown to inhibit the oxidation of LDL induced by activated neutrophils and macrophages at concentrations greater than 40 μmol/L (Scaccini and Jialal, 1994). Adhesion of mononuclear cells to endothelium, an early event in atherogenesis, was lowered in smokers with high levels of vitamin C (2000 mg/day) (Weber *et al.*, 1996). Vitamin C has also been shown to improve endothelial function and vasodilation through its antioxidant activity, which weakens the synthesis of nitric oxide (Esper *et al.*, 2006). Plasma ascorbic acid has also been shown to be inversely associated with blood pressure (Choi *et al.*, 1991). There is also evidence of protection against cataracts. In one case-control study, of subjects with cataract versus controls, vitamin C intakes > 490 mg/day were associated with a 75% lower risk of cataracts compared with intakes < 125 mg/day (Jacques and Chylack, 1991). There is some epidemiologic evidence of a protective effect against non-hormone-dependent cancers (Block, 1991). Because of the early focus on the common cold, vitamin C has been extensively studied in relation to immune function. However, results have been mixed, possibly because most studies have been done in populations with generally adequate vitamin C concentrations prior to supplementation.

Several studies of apparently healthy elderly populations in the United States have not found declines in plasma ascorbate with older age (Garry *et al.*, 1987;

Jacob *et al.*, 1988). Further, a metabolic study of renal tubular reabsorption and excretion of ascorbic acid in healthy elderly and young adults found no differences in renal handling of the vitamin by age group (Oreopoulos *et al.*, 1993). Low blood vitamin C concentrations in institutionalized and chronically ill elderly have been ascribed primarily to poor intake (Newton *et al.*, 1985), although impaired intestinal absorption has also been suggested (Davies *et al.*, 1984).

20.12 Conclusions

Evidence of the critical importance of nutrition in protecting against the development and progression of chronic conditions with ageing continues to mount. Because older adults have lower energy requirements, the need for a nutrient-dense diet is critical. The water-soluble nutrients, with the exception of vitamin B_{12}, are not stored in the body, and need to be replaced daily. There is evidence that many older adults do not obtain adequate intakes of several of these vitamins. Although in many countries thiamin, riboflavin and niacin are added back to most refined flour products, preventing the occurrence of deficiency, these may not be consumed in adequate amounts if total dietary intake is low. Further, most riboflavin is obtained from dairy products and may be low in many elderly individuals who do not consume milk.

Recent research has highlighted the particular importance of vitamins B_6, B_{12} and folate in the maintenance of low homocysteine concentrations. The latter metabolite has been implicated in vascular disease and associated with incidence of heart disease, stroke and cognitive impairment. Unlike the first three B vitamins, these have not been added to enriched flour until the recent addition of folic acid to cereal grain products in the United States and some other countries. Pre-fortification, and still in countries without this fortification, folate intakes and low plasma concentrations have been common in the older population and a cause for concern. Vitamin B_{12} deficiency remains an important and prevalent problem in elderly populations, even when intakes appear to be adequate, due to a high frequency of impaired absorption. Several medications, including widely prescribed acid blockers, are exacerbating this problem. For this reason, the use of foods fortified with vitamin B_{12}, such as commercial breakfast cereals, or the use of vitamin B_{12} supplements is recommended for adults over the age of 50 years. In the absence of atrophic gastritis or medication interference, the USRDA of 6 μg, the amount in most vitamin preparations, should be adequate for most individuals. Because many people are unaware of these conditions, most senior formulas add 25 μg for daily use. However, once deficiency is present, up to 1000 μg per day may be needed. For this reason, it is important to have plasma vitamin B_{12} tested before deciding on dosage. Vitamin B_6 has received less research attention, but has long been associated with immune function and has recently been associated with mood disturbances and cognitive decline. This vitamin is also frequently consumed in less than adequate amounts

by the older population. Finally, although easily obtained from fruit and vegetables in a healthy diet, vitamin C is an important nutrient for which there is mounting evidence of importance in older age, while intakes may be inadequate.

The results of many supplementation trials with single nutrients have demonstrated that, short of actual deficiency, it appears best to obtain adequate intakes of vitamins though food, where they are packaged together with phytonutrients and other food constituents for optimal action. This means that, with lower total energy intake in the ageing population, food choices must be made to optimize nutrient density, ideally using a variety of as much whole and fresh food as possible. Due to functional impairment, chronic conditions and other limitations, it is not always possible for elderly individuals to consistently obtain and prepare an ideal diet. For this reason, the use of a multivitamin supplement will ensure that adequate vitamin intakes are obtained. For those aged 50 years and above, senior formulations, which contain more vitamin B_{12} and less iron than standard formulas, are recommended, and for those with absorption problems or low plasma vitamin B_{12}, additional vitamin B_{12} supplements may be advised. However, the importance of additional chemical compounds in foods is beginning to be widely recognized, and despite the use of a supplement, fresh fruit, vegetables, low-fat dairy products and whole grains should continue to be emphasized whenever possible.

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21

Phytoestrogens and the health of older women

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Abstract: Several health benefits have been ascribed to dietary oestrogens isoflavones and lignans, the so-called phytoestrogens, because of their capability to bind to the oestrogen receptor. After addressing what phytoestrogens are and in which foods they occur, the chapter will provide the current evidence for effects on cardiovascular disease risk, breast cancer risk, bone health and cognitive function. For definitive answers, randomised clinical trials are needed, which are still lacking. For isoflavones, effects may differ depending on timing of exposure and capability to produce the more active metabolite equol.

Key words: isoflavones, lignans, cardiovascular disease, breast cancer, bone, cognitive function.

21.1 Introduction

Over recent decades there has been growing interest in the scientific as well as in the lay press for phytoestrogens, plant compounds with a structure comparable to the female sex hormone 17β-oestradiol. Several health benefits have been ascribed to phytoestrogens, firstly because of their presumed oestrogenic or anti-oestrogenic properties, but later also because of other effects, including anti-oxidant. In this chapter we present the current evidence for beneficial health effects of phytoestrogens.

This chapter starts with a general background on phytoestrogens: what are phytoestrogens, which phytoestrogens occur in Western diets, and which foods contribute most to the intake of these phytoestrogens? Also, the assumed

mechanisms of action are described. Next, the evidence from human studies, including observational studies as well as clinical trials, regarding health benefits of phytoestrogens will be discussed. Since phytoestrogens have a structural similarity to oestradiol, most of the phytoestrogen research has focused on oestrogen agonist and antagonist effects, and also on diseases that occur in women. Because most of the evidence has been accrued for female health, this chapter will concentrate on diseases that are relevant for female health and disease, including cardiovascular disease, breast cancer, bone density, and cognitive function. The chapter concludes with a short commentary on future trends and sources of further information.

21.2 Phytoestrogens

Phytoestrogens are chemicals occurring in plant foods that are structurally comparable to the female sex hormone 17β-oestradiol. The compounds have the capacity to bind to the oestrogen receptor, but there is not only large variation in relative binding affinity between compounds, but also the relative receptor binding affinities differ for oestrogen receptor (ER)-alpha and ER-beta.

There are four main classes of phytoestrogens: isoflavones, coumestans, lignans, and the prenylflavonoid (or flavonones), all occurring in either plants or in their seeds. Most isoflavones occur in plants in the bound form of their glucosides, daidzin, genistin and glycitin, and are biologically inactive. After consumption of isoflavones by humans, hydrolysis takes place at the intestinal brush border and heterocyclic phenols with a structure similar to oestrogens are formed by complex enzymatic metabolic conversions in the gastrointestinal tract. The efficiency of this conversion affects bioavailability, and subsequent metabolism. The isoflavones daidzein and genistein may also be derived from their precursors biochanin A and formononetin. Daidzein is eventually metabolised to both equol and O-desmethylangolensin (O-DMA). Genistein is metabolised to 6′hydroxy-O-DMA. Coumestrol and 4′-methoxycoumestrol are the most important coumestans with oestrogenic activity in human food.

The oestrogenically active lignans enterodiol and enterolactone, are derived from the compounds secoisolariciresinol (SECO) and matairesinol (MAT), which are derived from their precursors lariciresinol (LARI), pinoresinol (PINO), that occur in plant foods in larger quantities than SECO and MAT. SECO and MAT are converted by human gut bacteria to the human lignans enterolactone (ENL) and enterodiol (END). Figure 21.1 shows structures of the isoflavones biochanin A, formenonetin, daidzein and genistein, the lignans MAT and SECO, and oestradiol as the natural oestrogen.

Isoflavone and lignan absorption and utilisation require a series of de-conjugation and conjugation steps. After utilisation, conjugated isoflavones and lignans are excreted into urine as well as into bile. After excretion into the latter, de-conjugation by gut bacteria and re-absorption may take place, resulting in further metabolism and degradation in the intestine. Concentrations of the

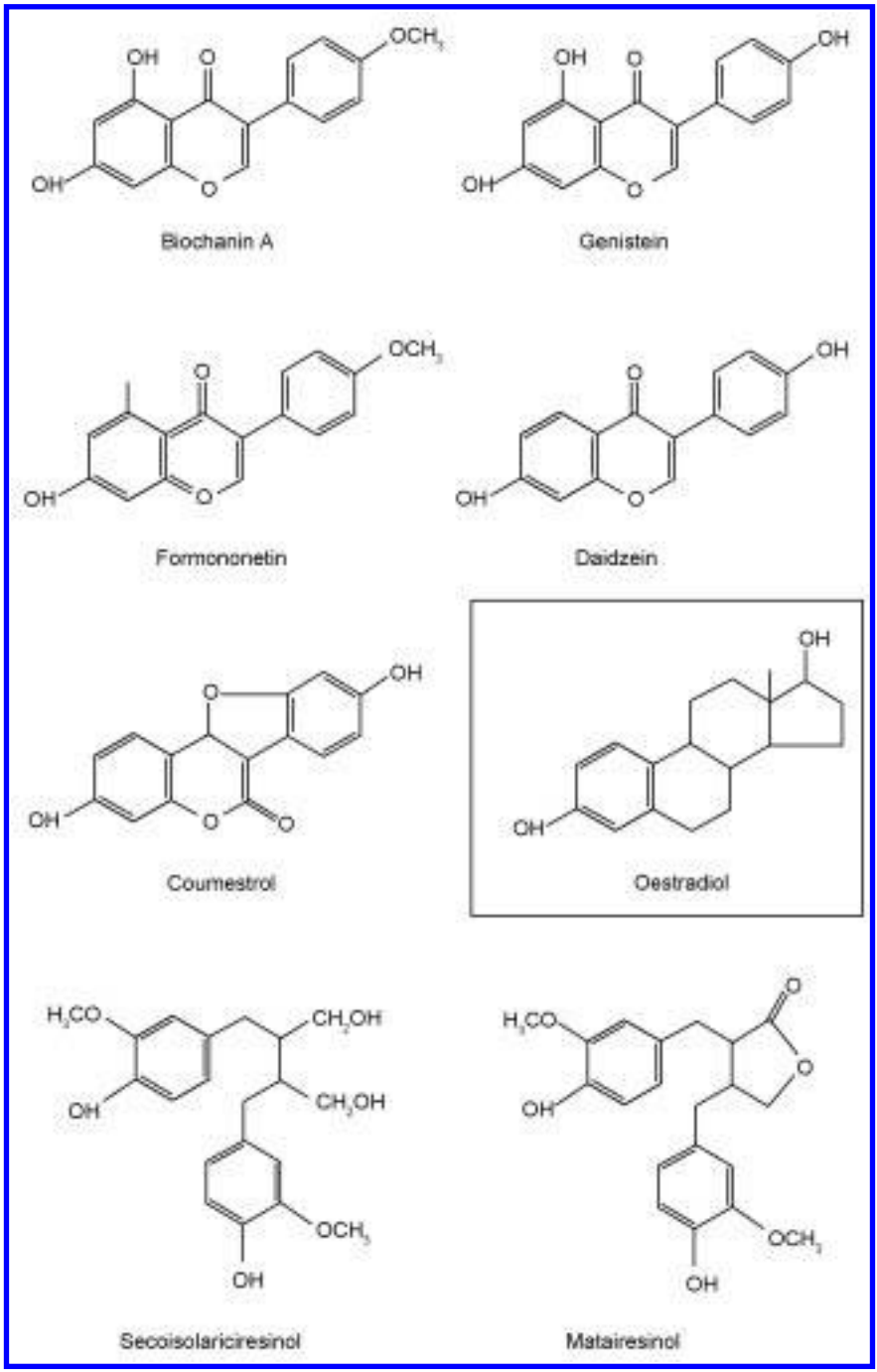

Fig. 21.1 Chemical structures of isoflavones, lignans, and oestradiol.

various phytoestrogen metabolites vary widely between individuals, although excretion of metabolites is generally highly correlated with dietary intake.

21.2.1 Isoflavones

Food sources

Phytoestrogens are found in various plants including grains, beans, green vegetables, fruits, nuts, and grasses. Isoflavones are primarily found in soybeans and soy foods. These contain approximately 0.2–1.6 mg of isoflavones/g dry weight. Chickpeas and other legumes, such as mung beans and champignons, and clover are other isoflavone sources. From published information on urinary phytoestrogen excretion in humans, it is clear that soybean consumption is only significant in populations in the Far East. The mean daily isoflavone intake in Asian populations has been estimated to be approximately 30 mg/day.

In Western populations, beans and peas (45%), tea and coffee (25%), nuts (10%), and grains, rice and cereals (5%) are the main sources of isoflavone intake (Table 21.1). The mean intake of isoflavones is approximately 1 mg/day in omnivores and several mg/day in vegetarians (de Kleijn, 2001; Boker, 2002; Ritchie, 2006).

Mechanisms of action

Isoflavones are suggested to be involved in both genomic and non-genomic mechanisms in exerting effects on human health (Anderson, 1999). Isoflavones are able to interact with enzymes and receptors, and because of their stable structure and low molecular weight they can pass through cell membranes (Adlercreutz, 1998). These interactions allow them to bind to ERs, which initiates dimerisation of the receptor and interaction with oestrogen response elements on DNA (Kuiper, 1996; 1997; 1998). Activation or inhibition of gene transcription results in altered protein expression. Whether this results in oestrogenic agonistic or antagonistic effects seems to depend on the background oestrogen concentration (Hwang, 2006).

Besides genomic effects, isoflavones are also considered to have non-genomic effects. Genistein has been shown to inhibit carcinogenesis in animal models. There is a growing body of experimental evidence showing that the inhibition of human cancer cells by genistein operates through the modulation of genes that are related to the control of cell cycle and apoptosis. Examples of these inhibitory actions of genistein include the inhibitory effect of genistein on protein tyrosine kinases, whose actions are crucial to the control of cellular growth and apoptosis (Akiyama, 1987) and the inhibition of the activation of NF-kappa B and Akt signaling pathways, both of which are known to maintain a homeostatic balance between cell survival and apoptosis (Gong, 2003). Isoflavones are also suggested to inhibit DNA topoisomerase (topo) II by stabilising the cleavable complex (Constantinou, 2002), and to suppress angiogenesis (Ambra, 2006; Gamble, 2006).

Isoflavones also have antioxidant effects due to their phenolic structure (Kurzer, 1997). Genistein, daidzein and equol are more effective antioxidants

Table 21.1 Intakes of phytoestrogen by food groups by Dutch women (% daily intake)

Food group	Daidzein	Genistein	Formononetin	Biochanin A	Coumestrol	Matairesinol	Secoisolariciresinol
Vegetables	31.8[a]	31.0[a]	49.8[a]	35.2	97.2[a]	6.4	8.2
Peas/beans	28.6	25.7	49.8	35.2	62.2	<0.1	0.3
Potatoes	2.1	4.1	–	–	–	4.8	5.6
Leafy vegetables[b]	0.6	0.4				1.1	1.9
Other	0.5	0.8	<0.1	–	35.0	0.5	0.4
Fruit	4.3	2.1	–	–	–	3.6	1.0
Berries	0.1	0.8				2.8	4.1
Non-berries	4.2	1.3				0.8	9.9
Fruit/vegetable juice	1.5	<0.1	–	–	–	0.3	1.6
Fruit juices	1.0	<0.1				0.2	1.5
Vegetable juices	0.5	<0.1				0.1	0.1
Coffee/tea	16.3	4.8	24.3	–	–	12.2	22.8
Coffee	14.5	4.8	24.3			–	15.8
Tea	1.8	–	–			12.2	7.0
Traditional soy foods	6.5	6.5	–	–	–	–	–
Breakfast cereals	17.2	14.4	0.1	0.1	0.2	7.0	0.1
Grain products	15.5	11.9	6.2	0.1	2.3	62.9[a]	40.8[a]
Bread	15.4	11.8	6.2	0.1	2.3	54.2	40.7
Cakes/cookies	0.1	0.1	–	–	–	5.5	<0.1
Pasta/rice	–	–	–	–	–	3.2	0.1
Nuts (mostly peanuts)	3.8	16.2	2.1	45.0[a]	–	0.1	4.8
Alcohol	<0.1	<0.1	<0.1	–	–	6.4	1.3
Other	3.1	13.1	17.5	19.6	0.3	1.1	6.4
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

[a] Main sources (by food groups) for isoflavones, coumestans and lignane intake.
[b] Leafy vegetables – cabbage/lettuce/chicory/endive/spinach.
Reproduced from Boker LK, Van der Schouw YT, De Kleijn MJ, Jacques PF, Grobbee DE, Peeters PH. Intake of dietary phytoestrogens by Dutch women. *J. Nutr.* (2002) 132: 1319–28 (Boker, 2002) with permission of the American Society for Nutrition

than vitamin C and quercetin, also in physiologic ranges (Rufer, 2006). Other effects can take place at the cellular and molecular level and potentially influence the biosynthesis and metabolism of steroids and fatty acids, the serum steroid carrier proteins (sex steroid binding proteins and α-fetoprotein), and the intracellular and transmembrane transfer of hormones to a membrane and to nuclear receptors (Martin, 1996; Benassayag, 2002).

Isoflavones inhibit the enzymes needed for hormone conversions, which may reduce cancers by lowering the biological activity of sex hormones in target organs (Adlercreutz, 1998).

21.2.2 Lignans

Food sources

Lignans are found in seeds, such as flaxseed, linseed, sunflower seeds, and pumpkin seeds, grains, such as oat, wheat, barley, and rye, and other vegetables, such as carrots, garlic and broccoli. It can also be found in peanuts, tea and coffee. Lignan consumption is more widespread in Western populations, due to the more widespread occurrence of lignans in common foods but studies on intake levels are still scarce. Fruits (25%), vegetables (20%), berries (15%), grains, rice and cereals (10%), tea and coffee (10%) and nuts (10%) are the main sources of lignan intake (Milder, 2005; Thompson, 2006).

Mechanisms of action

Although there is no direct evidence that lignans bind to the oestrogen receptor, both enterolactone and enterodiol have oestrogenic as well as anti-oestrogenic activities (Wang, 2002). There are several suggestions that lignans induce sex hormone binding globulin (SHBG) production, which lowers free oestradiol concentrations because it is bound to SHBG (Adlercreutz, 1987; Schottner, 1998). This may be a mechanism though which lignans exert beneficial effects on breast cancer risk, as higher oestradiol levels are a main risk factor. Recently it was shown that ENL and END inhibit the activity of the necessary enzymes for oestrogen synthesis aromatase and 17β-hydroxysteroid dehydrogenase type 1 in MCF-7 cancer cells, thereby decreasing the amount of oestradiol produced and consequently cell proliferation (Brooks, 2005).

21.3 Cardiovascular disease

21.3.1 Introduction

Coronary heart disease, also ischaemic heart disease, comprise diseases of the heart and blood vessels that are the result of atherosclerosis. This results in ischaemia in the cardiac muscle. Coronary heart diseases are categorised as acute (myocardial infarction) and chronic (angina pectoris) forms. Myocardial infarction occurs when an embolism suddenly occludes a coronary artery, causing ischaemia in the area of the cardiac muscle served by that artery, and finally necrosis, resulting in loss of cardiac muscle. When the damage is large,

the pump function of the heart is compromised and heart failure occurs. Narrowing of the coronary arteries can also lead to temporary ischaemia, for example when exercising, this is angina pectoris. Coronary heart disease is the main cause of morbidity and mortality in Western countries; in the Netherlands, the prevalence is 33 per 1,000 women, on an annual basis 15 per 10,000 women experience myocardial infarction, and 7 per 10,000 women die of coronary heart disease (RIVM, 2006).

Lifestyle factors play a very important role, in particular diet, smoking and exercise. These factors affect physical parameters such as serum cholesterol, blood pressure, overweight, diabetes mellitus and haemostasis. Furthermore, chronic low-grade inflammation plays a major role in coronary heart disease.

21.3.2 Isoflavones

Soy isoflavones have strong biological properties in animals, causing arterial vasodilation, lowering serum cholesterol (Anthony, 1998), and inhibiting atherosclerosis in postmenopausal monkeys (Clarkson, 2001). Isoflavones remain in soy protein preparations that are not extracted with alcohol. During the preparation of soy protein isolate, the soy is washed with alcohol, removing a substantial amount of the isoflavones.

Subsequent to a meta-analysis of effects of soy protein on lipid levels in humans by Anderson *et al.* (1995), many well-controlled studies explored the lipid-lowering effects of soy protein with greater specificity, in particular with a focus on isoflavones (Adlercreutz, 1997; Anthony, 1998).

In the meta-analysis published by Anderson *et al.* (1995), a strong gradient of LDL cholesterol reduction was found among studies according to initial cholesterol levels. In the studies published afterwards, doubt was cast on the dose-response effect of soy or isoflavones on lowering of lipid levels.

In 2006, the Nutrition Committee of the American Heart Association published a Science Advisory for Professionals, in which the available evidence for beneficial cardiovascular effects of isoflavones reported after the first meta-analysis by Andersen was reviewed (Sacks, 2006). First, the evidence on soy protein containing isoflavones is reviewed. In 22 randomised trials, *isolated soy protein with isoflavones* was compared with *another type of protein*, such as casein (milk protein), wheat protein, or mixed animal proteins. A wide range of isoflavone contents was used, varying from 40 to 318 mg in 25 to 135 g/d of protein. LDL or non-HDL cholesterol concentrations decreased in most studies, statistically significantly in eight, with an overall effect of ~3% (weighted average). This finding is corroborated in a recent meta-analysis that included 10 studies published from 1995 to 2002, where also no dose-effect was found (Weggemans, 2003). Over all studies, there is no apparent dose effect; the eight studies with 50 g of soy protein showed a drop in LDL cholesterol concentration similar to those using a smaller amount of soy, ~3% overall, which was also corroborated by Weggemans (2003). The cut-point for daily soy protein intake, 50 g, defines a large amount, more than half of the daily average total protein

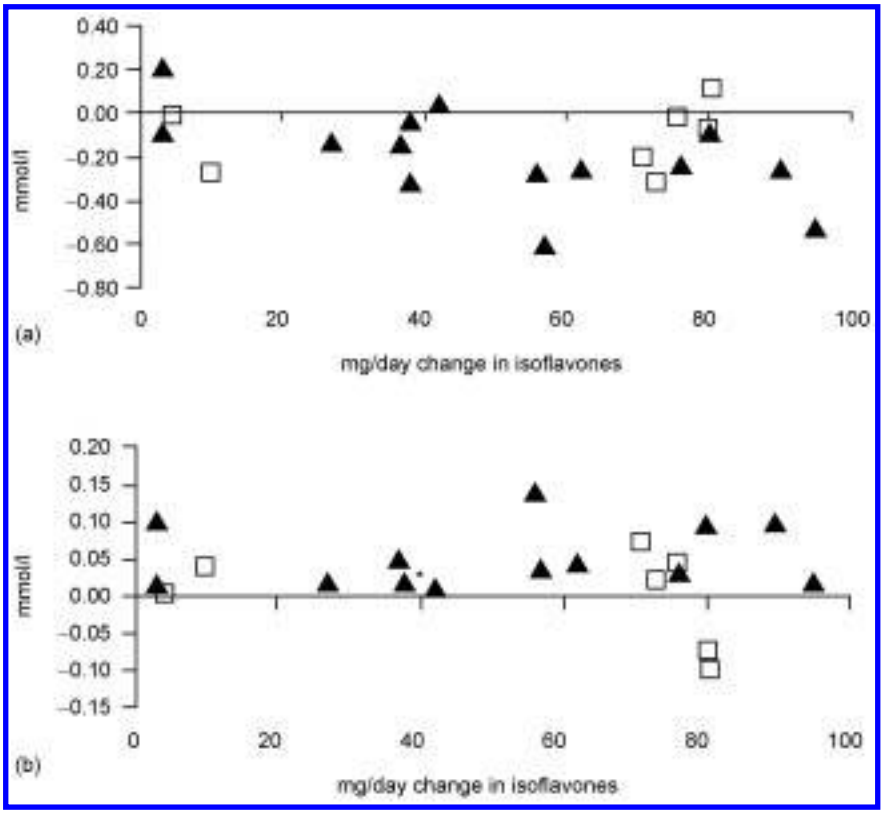

Fig. 21.2 Change in (a) plasma LDL cholesterol (mmol/l) and (b) plasma HDL cholesterol (mmol/l) as a function of the change in soy associated isoflavones (mg) in studies fulfilling the very stringent and the general selection criteria. *Indicates a data point that represents two independent observations. Reproduced from: Weggemans RM, Trautwein EA. Relation between soy-associtated isoflavones and LDL and HDL cholesterol concentrations in humans: ameta-analysis. *Eur J Clin Nutr* (2003) 57: 940–946 (Weggemans, 2003), with permission of Macmillan Publishers Ltd.

intake in the Netherlands. No significant effects were evident for HDL cholesterol or triglycerides in most of the studies; the weighted average effects were very small: 1.5% for HDL cholesterol and 5% for triglycerides. The effects of isoflavones on LDL and HDL cholesterol are nicely illustrated in Fig. 21.2.

Some studies compared soy protein that did with soy protein that did not contain isoflavones, whereas other studies tested isoflavones in pill form as compared with placebo. Again a wide range of isoflavone amounts was studied. One study compared the effect of isoflavones provided with either soy or animal proteins. Among 19 studies, only three showed significant reductions in LDL cholesterol concentration, and the effect among all studies (weighted average) was nil, 0%. Changes in HDL cholesterol and triglycerides were not significant and showed no trend toward an effect of isoflavones. Despite large increases in blood isoflavone concentrations, there is no indication of a dose effect on blood lipids.

Other cardiovascular risk factors have been studied less frequently, but for lipoprotein(a), an LDL-like lipoprotein that is an independent predictor of CVD, and blood pressure the AHA Nutrition Committee was able to review the data (Sacks, 2006). Lipoprotein(a) was increased by soy protein in two studies and unchanged in nine others. However, isoflavones had no effect on lipoprotein(a) in six other studies, nor did soy protein that contained isoflavones (Sacks, 2006), so a beneficial effect of isoflavones on lipoprotein(a) is not very likely.

Several studies tested the effect of soy protein with isoflavones, as compared with casein or milk protein, on blood pressure. Blood pressure decreased significantly in one study but not in the other five studies. The weighted average change is 1 mm Hg systolic blood pressure. Several studies that evaluated the effect of soy isoflavones also did not find a significant effect on blood pressure (Sacks, 2006).

In conclusion, a lipid, lipoprotein or blood pressure lowering effect of isoflavones does not seem very likely.

21.3.3 Lignans

In animal studies lignans like sesamin reduce blood pressure, aortic superoxide production and improvement in endothelial dysfunction (Noguchi, 2001; Nakano, 2002; 2003).

Observational studies on effects of dietary intake of lignans on blood pressure also suggest beneficial effects (de Kleijn, 2002; Kreijkamp-Kaspers, 2004a). In one cross-over double-blind double-dummy randomised controlled trial with three different cultivars of flax seed containing varying amounts of lignans no differences were found for blood pressure. The greatest reduction in peripheral resistance was found with the high lignan variety, but this was statistically not significant. This flax seed also produced the greatest reduction in plasma cortisol during stress (Spence, 2003). However, recent randomised studies could not find any effect of a lignan complex isolated from flax on endothelial function (Hallund, 2006b) and on blood pressure (Stuglin, 2005).

In animal studies, effects of lignans on serum lipids are confusing; increases in triglycerides as well as short-term decreases in total and LDL-cholesterol and decrease of aortic atherosclerosis have been reported (Prasad, 1998; 1999). Results in humans are rather mixed, with several well-designed studies finding no effects on serum lipids (Hallund, 2006a; Tarpila, 2002; Stuglin, 2005; Lemay, 2002), whereas other find lipid-lowering effects (Wu, 2006; Lucas, 2002; Bierenbaum, 1993).

With regard to clinical manifest endpoints, such as myocardial infarction or cardiovascular mortality, only observational studies are conducted. In a Finnish population a case-control study nested in a prospective cohort was performed with acute coronary events as endpoint. Higher serum enterolactone levels at baseline were associated with a statistically significant 35% reduced risk, although it is questionable whether healthy behaviour was effectively taken into account in the analysis (Vanharanta, 1999; 2003). In the same population, a

protective effect of higher baseline enterolactone levels on coronary heart disease and cardiovascular disease mortality was also found (Vanharanta, 2003). One prospective study on dietary lignan intake in the Netherlands could not find an effect on cardiovascular disease risk (van der Schouw, 2005), but another cohort study from the Netherlands found a 20% reduction of coronary heart disease, cardiovascular disease, and all cause mortality, which was restricted to matairesinol intake (Milder, 2006).

Overall, the data do not seem solid enough to advise women to increase lignan intake, although the increase of lignan-rich foods is beneficial for health for their contents of vitamins and fibre.

21.4 Breast cancer

21.4.1 Introduction

With 1 million new cases in the world each year, breast cancer is the commonest malignancy in women and comprises 18% of all female cancers. In the Netherlands, where the age standardised incidence and mortality is among the highest in the world, the incidence among women aged 50 approaches 15 per 10,000 women per year, and the disease is the single commonest type of cancer in women. In the Netherlands, one in nine women will get breast cancer during her life. Ten-year survival increased from 30% in the 1960s to 70% in 2000, due to national breast cancer screening programs, better chemotherapy and hormone therapy (RIVM, 2006).

Age adjusted incidence and mortality for breast cancer varies by up to a factor of five between countries. The difference between Far Eastern and Western countries is diminishing but is still about fivefold. Studies of migrants from Japan to Hawaii show that the rates of breast cancer in migrants assume the rate in the host country within one or two generations, indicating that environmental factors are of greater importance than genetic factors (McPherson, 2000). Diet could be an important environmental factor determining breast cancer risk.

Breast cancer risk is partially determined by several hormone-related factors, such as age at menarche, parity, and age at menopause, and a pooled analysis of nine prospective studies showed that high levels of endogenous sex hormones, especially oestrogens, may increase breast cancer risk (Key, 2002). This knowledge helped fuel the research into the effects of phytoestrogens on breast cancer risk.

21.4.2 Isoflavones

The observation that breast cancer incidence was low in countries where per capita soy intake was high fuelled the research on the hypothesis that soy, and isoflavones in particular protect against breast cancer (Adlercreutz, 1997). Animal studies have generated conflicting data regarding the ability of genistein or soy to reduce mammary tumorigenesis, and some even suggested breast cancer risk increasing effects (Messina, 2006).

Recently, a meta-analysis was performed of 18 epidemiologic studies (12 case-control and six cohort or nested case-control) published from 1978 through 2004 that examined soy exposure and breast cancer risk (Trock, 2006). These 18 studies were very different in the parameters that were chosen as measures of isoflavone intake. Frequency of tofu (or soybean curd) consumption, soy protein intake, urinary excretion of isoflavones, total or individual dietary isoflavone intake, a combination of urinary and dietary isoflavones, and both tofu intake during adolescence and isoflavone intake during adulthood were reported and combined in the meta-analysis. Risk estimates, levels and measures of soy exposure, and control for confounding factors varied considerably across studies. In a pooled analysis, among all women, high soy intake was modestly

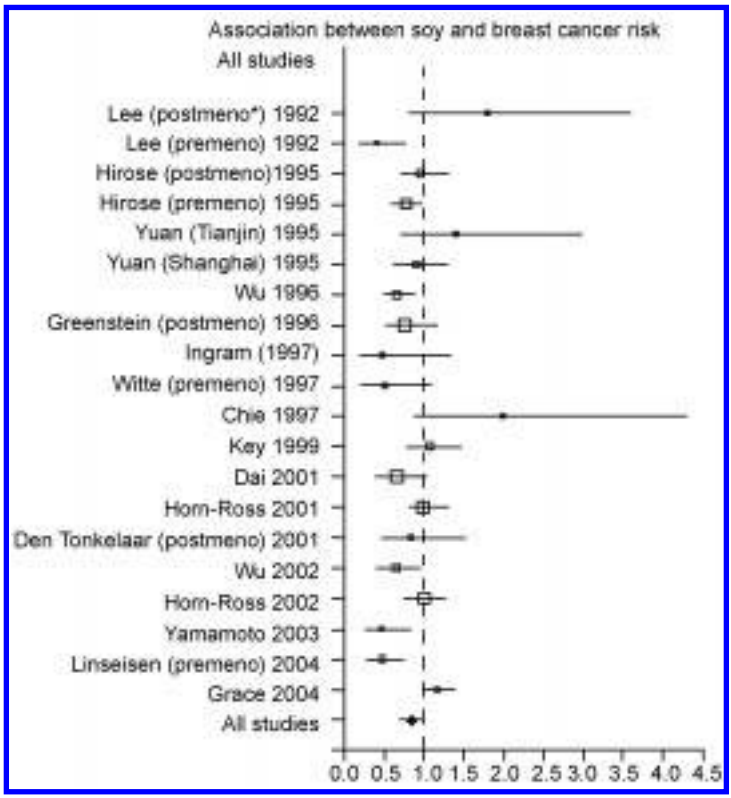

Fig. 21.3 Association between soy exposure and breast cancer risk in all studies in this meta-analysis. Relative sample sizes are indicated by size of symbols, with increasingly large symbols representing studies with 200 case patients or fewer, 201–400 case patients, 401–600 case patients, 601–1000 case patients, and more than 1000 case patients. Horizontal lines represent 95% confidence intervals for the odds ratios. OR = odds ratio; RR = relative risk; premeno = premenopausal women, postmeno = postmenopausal women. Reproduced from Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk. *J Natl Cancer Inst* (2006) 98: 459–71 (Trock, 2006) with permission of first author.

associated with reduced breast cancer risk (odds ratio [OR] = 0.86, 95% confidence interval [CI] = 0.75 to 0.99); the association was not statistically significant among women in Asian countries (OR = 0.89, 95% CI = 0.71 to 1.12) (Fig. 21.3). Among the 10 studies that stratified by menopausal status the inverse association between soy exposure and breast cancer risk was somewhat stronger in premenopausal women (OR = 0.70, 95% CI = 0.58 to 0.85) than in postmenopausal women (OR = 0.77, 95% CI = 0.60 to 0.98); however, eight studies did not provide menopause-specific results, six of which did not support an association. When exposure was analysed by soy protein intake in grams per day, a statistically significant association with breast cancer risk was seen only among premenopausal women (OR = 0.94, 95% CI = 0.92 to 0.97) (Fig. 21.4).

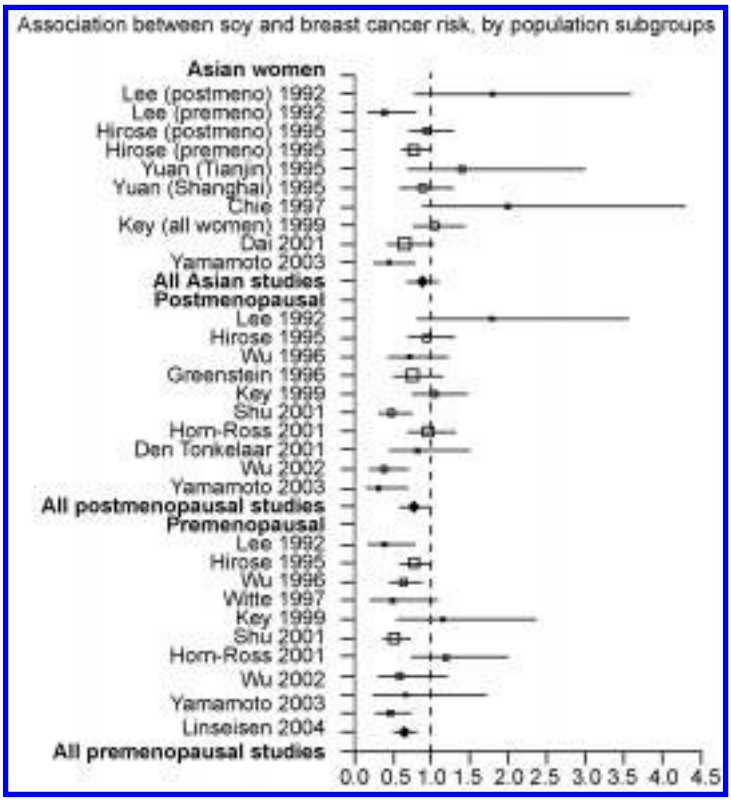

Fig. 21.4 Association between soy exposure and breast cancer risk, by population subgroups. Relative sample sizes are indicated by size of symbols, with increasingly large symbols representing studies with 200 case patients or fewer, 201–400 case patients, 401–600 case patients, 601–1000 case patients, and more than 1000 case patients. Horizontal lines represent 95% confidence intervals for the odds ratios. OR = odds ratio; RR = relative risk; premeno = premenopausal women, postmeno = postmenopausal women. Reproduced from Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk. *J Natl Cancer Inst* (2006) 98: 459–71 (Trock, 2006) with permission of first author.

21.4.3 Lignans

Lignans have been studied less extensively than isoflavones in relation to breast cancer risk. Controlled clinical trials have not been performed, but observational studies have. Ten case-control studies published until 2004 have been reviewed in a recent paper (Boccardo, 2006). Some other epidemiological studies were not included in this review, but are discussed below as well. As for isoflavones, lignan exposure was also estimated in several ways. Some studies investigated dietary intake, some urinary excretion of enterolactone, and others measured lignans in blood samples. Several classical case-control studies have been performed, of which the majority tends to find a protective effect of higher lignan levels on breast cancer risk which is in some studies confined to premenopausal women (Boccardo, 2006; Piller, 2006a). The nested case-control studies, with collection of exposure information before the breast cancer diagnosis, are null (Hulten, 2002; Grace, 2004) or inconclusive (reviewed in Boccardo, 2006), but in the latter, effect estimates tend to be greater than 1, i.e. indicative of an increased risk. Two cohort studies were published, which were also inconclusive, but effect estimates tended to be less than 1, indicating a protective effect (Keinan-Boker, 2004; Boccardo, 2006). Other studies suggest that a protective effect of lignans is depending on the oestrogen receptor status of the breast cancer (McCann, 2006), or on single nucleotide polymorphisms (SNPs) in genes involved in oestrogen metabolism (McCann, 2002; Piller, 2006b). All in all, the evidence regarding lignans and breast cancer risk is inconclusive.

21.5 Bone health

21.5.1 Introduction

Bone mineral density (BMD) is a composite of bone mineral content (BMC) and cross-sectional area of bone. Both BMD and BMC measurements are thought to be the best approach for screening individuals with risk of osteoporosis and the major determinant of fracture risk. Other factors affecting fracture risk are the bone turnover rate and the microarchitecture of the bone. BMD and BMC measurements, however, do not measure the actual bone turnover and a long follow-up time is required to detect any change. Bone turnover can be estimated from various biomarkers of bone formation (serum osteocalcin, total and bone specific alkaline phosphatase, procollagen type I carboxy terminal propeptide, and procollagen type I amino terminal propeptide) and that of bone resorption (urinary hydroxyproline, galactosyl hydroxylysine, total and free pyridinoline, total and free deoxypyridinoline, collagen type I cross-linked N-telopeptide, and collagen type I cross-linked C-telopeptide, tartrate resistant acid phosphatase, and serum type I collagen carboxy terminal telopeptide) (Lane, 2006), which are often used in short-term studies evaluating preventive or therapeutic strategies.

21.5.2 Isoflavones

Most of the rodent studies have demonstrate a positive effect of isoflavones on bone, but some started supplementation very early in life, or, when intended to be a model for postmenopausal women, immediately, or very soon, after ovariectomy. In humans, findings based on clinical trials examining the effects of isoflavones on bone health for a period of one year or less have been inconsistent, but generally suggest that isoflavones can attenuate bone loss in perimenopausal and in younger postmenopausal women. Our own work suggests that postmenopausal women may not benefit anymore when they are several years past menopause (Kreijkamp-Kaspers, 2004b). Therefore, the rodent model is probably mainly used in a situation when ER number is less likely to be as adversely affected or down-regulated by the lack of circulating E2. In 2004 a meta-analysis of the available evidence was published. It reported that fifteen clinical trials could be identified that examined the effects of isoflavones or isoflavone-rich soy protein on bone mineral density. In four trials, the intervention was isolated soy protein, seven used isolated isoflavones, and one each used soyflour, soymilk, soyfoods, or an isoflavone-rich soy extract. In the intervention group, isoflavone (in aglycone units) exposure from any source ranged widely from 37 to 150 mg per day. Most trials were conducted for 1 year or less and involved relatively few (<30) participants per group. The findings from these studies are inconsistent but generally suggest that isoflavones reduce bone loss in younger postmenopausal women. results overall suggest that isoflavones exert skeletal benefits in younger postmenopausal women (Table 21.2). Nearly half of the trials demonstrated statistically significant effects, although in two of these, this was the case only when comparing final results with baseline values, not when comparing final BMD among groups. One trial employing regression analysis indicated that isoflavone-rich soy protein had a significant positive effect on percentage change in BMD (5.6%) and BMC (10.1%), whereas there was no effect in either isoflavone-poor soy protein or whey protein control groups. The major limitation of the data is the short duration of the trials: to best predict likely long-term effects of any bone-active treatment, changes in BMD should be monitored over a 2–3-year period (Messina, 2004).

Similarly, the limited epidemiologic data generally show that among Asian populations isoflavone intake is associated with higher bone mineral density (Table 21.3). However, some caution is needed when drawing conclusions about the epidemiologic studies, not only because the data are limited, but because there may be publication bias. Asian epidemiologic studies that did not find relationships between soy intake and BMD that were published prior to the interest in the skeletal effects of isoflavones may not have reported these data. There is clearly a need for additional epidemiologic research, especially prospective studies that include not only BMD as an outcome, but also fracture rates. Because soy intake in the West is extremely low at this time, such research will need to be conducted among Asian populations that exhibit sufficient variation in soyfood intake (Messina, 2004).

Table 21.2 Clinical trials examining the effect of soy or isoflavone supplements on bone mineral density, bone mineral content, or bone stiffness

Study	Number per group	Age (years)		Study length	Study design	Findings	Comments
		Range	Mean				
Potter [15], USA	22	39–83	60	24 weeks	3 groups: 40 g CNFDM, 40 g ISP-56, 40 g ISP-90	No SS effects on total body and femur BMD or BMC, or spinal BMC Spinal BMD ↓ 0.64%, 0.21% in the CNFDM, ISP-56 groups, respectively; but ↑ 2.24% ($P < 0.05$ versus CNFDM) in the ISP-90 group	ISP-90 baseline BMD considerably lower than the other groups
Alekel [30], USA	21–24	ND	50	24 weeks	3 groups: 40 g whey, 40 g ISP-4, 40 g ISP-80	In the ISP-80, ISP-4 and whey groups, spinal BMD ↓ 0.20% ($P = 0.012$), 0.66% and 1.28%, respectively; spinal BMC ↑ 0.62% ($P = 0.11$), amd ↓ 0.62% and 1.73%, respectively *P* values are versus baseline	Statistics based on comparisons bwteen final versus baseline rather than final values among groups
Fitzpatrick [52], USA	22	ND	58 PostM	1 year	2 groups: placebo and appr. IF 60 mg	SS ↓ ($P < 0.01$) in hip BMD in placebo but not in IF group No change in spinal BMD in other group IF ↑ bone turnover consistent with an anabolic effect	Results based on 43 subjects 72 subjects enrolled in the initial 6-month study
Gallagher [51], USA	14–17	40–62	55	9 months	3 groups: ISP-<4, ISP-52, ISP-96	Spinal, femoral neck BMD ↓ with time in all groups but there were no SS differences ISP-96, ISP-52 trochanter BMD ↓ with time whereas ISP-<4 BMD ↑ 0.35% ($P = -0.02$), 1.34% ($P = 0.002$) at 9 and 15 months, respectively	Serum isoflavones reflected IF intake Control group was ISP low but not devoid of IF Intervention ended at 1 y
Chiechi [54], Italy	53–58	39–60	53	6 months	3 groups: control, soy-foods (appr. 47 mg IF/day), HT	No SS differences among groups at final forearm cortical or trabecular BMD Suggestion of benefit in diet group for both measures Trabecular BMD ↓ ($P < 0.05$) in control group compared with baseline	Large (34/58) dropout rate in diet group No SS effect of HT on BMD HT: 30% transdermal oestradiol (TE, 50 μg), 56% TE + 2.5 mg NM, 14% TE + 5 mg NM 12 days/month
Morabita (53**) Italy	30	47–57	52	1 year	3 groups: placebo, 54 mg genistein, HT	In the placebo, genistein, HT groups, femoral BMD changed by appr. −0.7, 3.7, 2.4%, respectively; spinal BMD changed by appr. −1.5, 3.2, 4.0%, respectively Differences between genistein and HT groups and placebo SS ($P < 0.01$)	Effects on Ward's triangle similar to effects on femoral BMD
Uesugi [55] Japan	12,11	40–62	51	4 weeks	2 groups: placebo and 61.8 mg IF	Final calcaneous bone stiffness did not differ between groups Urinary pyridinoline ↓ in IF group ($P < 0.05$) and final value lower than placebo ($P < 0.05$) Urinary deoxypyridinoline ↓ in IF group ($P < 0.05$) but not different from placebo	IF supplement soy germ Dietary IF intake appr. 28 mg/day

Uesugi [56], Japan	10, 11	45–65	54	3 months	2 groups: placebo, 61.8 mg IF	Less than 1% change in spinal BMD versus baseline in both groups and no difference in final BMD between groups	IF supplement soygerm Background Japanese dietary isoflavone not reported but known to be appr. 25–50 mg/day
Dalais [29], Australia	appr. 15	45–65	54	12 weeks	Crossover 3 groups: 55 g/day wheat, soyflour (appr. 53 mg IF), or linseed	No SS effect on BMD 5.2% ↑ in total BMC in soy group compared with control	Magnitude of observed ↑ larger than for oestrogen and other anti-osteoporotic drugs
Chen [32*], Hong Kong	55–62	≤ 10 years menopause	54	1 year	3 groups: 0, 40, 80 mg IF	No SS effects on spinal or whole body BMD or BMC Yearly rate (%) of BMC loss at the total hip and trochanter for the 0, 40, and 80 mg groups was −0.17, −0.45, and 0.57, respectively, and −0.45, −1.45, and 1.08, respectively Differences were SS using either LSD or ANOVA versus placebo or mid-dose isoflavone group	Background dietary soy protein intake appr. 6 g/day Benefits mostly limited to women with lower (≤ median) initial BMD, BW (≤ median, 55.5 kg); calcium intake (≤ median, 1095 mg) and to women > 4 years since menopause
Hsu [31], Taiwan	37	40–57	51	6 months	No control 150 mg IF	No SS effects on calcaneus bone stiffness Spinal and hip BMD was not measured	No control group Did not control for background dietary IF intake
Lydeking-Olson [58], Denmark	22–23	≥ 1 year postM <75	58	2 years	4 groups: placebo (SC-1), SM-76, TP, and TP-SM-76	In the placebo, TP-SM-76, TP, and SM-76 groups, spinal BMD and BMC changed by −3.5 ($P = 0.006$), −3.0 ($P = 0.003$), −1.5, and +0.9%, respectively, and −3.8 ($P = 0.005$), −2.9 ($P = 0.03$), −0.2, and +0.6, respectively Statistical comparisons baseline versus final values No SS effects on femoral neck; change for the 4 groups was −0.2, 1.3, 0.9 and 0.5%	Findings suggest soy regardless of IF content may have reduced hip bone loss Analysis suggested soy was beneficial primarily only in equol producers
Yoles [57], Israel	39, 43	ND	56	12 months	2 groups: low (344 mg), high (644 mg) dose DT56a	Spinal and femoral neck BMD ↑ 3.6% amd 2.0%, respectively, in the high dose group but ↓ 0.6% in the low dose group Spinal and femoral neck BMD in high dose group versus baseline ($P = 0.039$) and low dose ($P = 0.037$) group was SS	No control Test compound not adequately described
Yamori [59], Brazil	20	45–59	53	10 weeks	2 groups: placebo and IF 37.3 mg	No SS change in right calcaneal bone stiffness	Bone stiffness was determined by an Achilles ultrasound bone densitomer
Kreijkamp-Kaspers [33**], The Netherlands	88	60–75	67	12 months	2 groups: 25.6 mg milk protein or ISP-99	No SS differences between groups at lumbar spine (L1-L4) or at most regions of the hip	Little bone loss occurred in either group; subjects were much older than subjects in all other trials

Notes: BW, body weight; CNFDM, casein, non-fat dried milk; ISP-x, isolated soy protein-mg isoflavones; SS, statistically significant; BMD, bone mineral density; BMC, bone mineral content; ND, no data; PostM, postmenopausal; appr., approximately; IF, isoflavones; HT, hormone therapy; NM, nomogestrol; SC-1, soy concentrate containing 1 mg IF; SM-76, soymilk containing 76 mg IF; TP, transdermal progesterone; DT56a, the generic name of a compound isolated from tofu that is said to contain multiple phytoestrogens.

Reproduced from Messina M, Ho S, Alekel DL. Skeletal benefits of soy isoflavones: a review of the clinical trial and epidemiologic data. *Curr Opin Clin Nutr Metab Care* (2004) 7: 649–58. Review (Messina, 2004), with permission of Lippincott Williams & Wilkins

Table 21.3 Results of selected epidemiologic studies investigating the relationship between soy or isoflavone intake and bone mineral density or stiffness

Study	*n*	Age (years)		Bone site	Findings	Comments
		Range	Mean			
Kimira [76], Japan	50	32–68	NI	Calcaneous	No relationship observed between bone stiffness and isoflavone intake	Intake assessed by 3-day dietary records
Tsuchida [33**], Japan	995	40–49	45	Second metacarpal	Calcium intake from soy products correlated ($P = 0.03$) with ↑ BMD after adjustment for age, height, body weight, and calcium intake Intake categories: 0–1, 2–5, 6–7x/week	FFQ focused only on major calcium sources Soy provided 21% of calcium FFQ not validated Specific soyfoods assessed not indicated
Horiuchi [74], Japan	85	52–83	67	Spine	Soy protein intake was positively correlated with spinal BMD, T-score and Z-score After controlling for energy, protein, and calcium, only soy protein was significantly ($P = 0.038$) associated with Z-score	Intake assessed by 3-day dietary record In stepwise multiple regression soy protein was positively ($P = 0.035$) associated with the suppression of bone resorption based on urinary deoxypyridinoline levels Median soy protein intake was 12.6 g/day
Somekawa [50], Japan	478	44–80	NI	Spine	BMD (g/cm^2) for intake (mg IF/day) categories of ≤35, 35–50, 50–65, 65> for early PMG was 0.865, 0.897, 0.931 and 0.933, respectively ($P < 0.001$) For late PMG, values were 0.806, 0.810, 0.873 and 0.877, respectively ($P = 0.01$) Correlation analysis showed estimated IF intake had a weak but SS positive corrleation with BMD adjusted for years since menopause and body weight ($r = 16$, $P < 0.01$)	Soy intake evaluated by dietary interview Average IF intake appr. 54 mg/day Positive correlation existed between BMD and the intake of fermented soybeans ($r = 0.22$; $P < 0.001$) and soybean curd ($r = 0.13$; $P < 0.01$) but not for soybean paste and fried soybean curd
Nagata [75], Japan	87	38–68	54	Calcaneous	No relationship observed between bone stiffness and soy product or isoflavone intake, or serum isoflavone levels	Semi-quantitative FFQ included 169 foods and nine questions about soyfoods
Katsuyama [77], Japan	117	PreM	32	Calcaneous	Low affinity vitamin D receptor (B allelel) was a risk factor for low bone stiffness Natto consumption among this group ($n = 29$) effective ($P = 0.04$) in maintaining BMD	Validated FFQ Soyfoods assessed other than natto not indicated but said to be unrelated to BMD Natto comparison > once per week versus no intake
Mei [78], Hong Kong	650	19–86	NI	Spine, hip, and Ward's triangle	No relationship between IF intake and BMD at any site among pre-menopausal ($n = 293$, average age, 37.5 years) women For postmenopausal women ($n = 357$, average age, 63.0 years) BMD at spine and Ward's triangle among the 1st, 2nd and 3rd intake tertiles was 0.771, 0.781 and 0.820, respectively ($P = 0.02$), and 0.415, 0.422, 0.450, respectively ($P = 0.05$)	FFQ included 33 foods, 9 of which were soyfoods Total hip BMD was not significantly related to IF intake but total hip T-score (low, mid, high tertiles: −2.051, −1.955 and −1.679) was ($P = 0.02$) Results for spine and Ward's triangle similar after excluding past and current HRT users
Ho [80], Hong Kong	116	30–40	NI	Spine	Average follow-up period 38.1 months 1st IF intake quartile spinal BMD ↓ 3.5% versus only ↓ 1.1% for 4th intake quartile Difference SS ($P < 0.05$) after adjusting for age, body size, height, and bone area Analysis suggested 15% of the IF effect due to calcium content of soy	Validated quantitative FFQ that included 73 food items with emphasis on calcium sources Mean 4th quartile IF intake appr. 15 mg/day Soyfoods (tofu and soymilk) assessed represent appr. 70% of total soy intake
Ho [79], Hong Kong	454	48–62	55	Spine, hip, total body	No relationship between soy protein intake and BMD at any site among women ($n = 269$) < 4 years since menopause Among women ($n = 185$) ≥ 4 years since menopause, BMD at the spine, hip, and total body was significantly lower among the 1st versus 4th soy protein intake quartiles	Validated quantitative FFQ extensively evaluated soy intake Mean IF intake among women ≥ 4 years since menopause 15.9 mg/day 1st-4th soy protein intake (g/day) quartiles: 1.45, 3.85, 6.97 and 19.78, respectively Excluding spine, there was a general trend for higher BMD/BMC with higher soy protein intake
Kim [81], Korea	75	52–65	58	Spine, hip, Ward's triangle	Urinary excretion of equol, daidzein, and genistein did not differ between women having normal bone status ($n = 25$), osteopenia ($n = 29$) or osteoporosis ($n = 21$) according to the lowest BMD at spine and femoral neck	Urinary excretion of the lignan enterolactone and the flavonoid apigenin was positively and negatively correlated with BMD, respectively

NI, not indicated; BMD, bone mineral density; FFQ, food frequency questionnaire; IF, isoflavone; PMG, postmenopausal group; SS, statistically significant; appr., approximately; PreM, pre-menopause; BMC, bone mineral content
Reproduced from Messina M, Ho S, Alekel DL. Skeletal benefits of soy isoflavones: a review of the clinical trial and epidemiologic data. *Curr Opin Clin Nutr Metab Care* (2004) 7: 649–58. Review (Messina, 2004), with permission of Lippincott Williams & Wilkins

The clinical data suggest that approximately 80 mg/day isoflavones are needed to derive skeletal benefits whereas the epidemiologic data suggest lower amounts are efficacious (Messina, 2004).

21.5.3 Lignans

The evidence regarding lignans and bone health is scarce. In 1998, data on a nested case-control sample from a 10-year follow-up study among 154 Dutch postmenopausal women were analysed. In this study, higher enterolactone excretion was associated with increased rate of bone loss, also after adjustment for confounders (Kardinaal, 1998). Later observational studies have not corroborated this finding (Kim, 2002; Hanna, 2004).

Several controlled clinical trials using flax seed as a rich source of lignans have also studied bone parameters as outcomes. In these trials, the duration of supplementation varied between three to four months and 12 months. None of these studies reported an effect of flax seed on blood and urinary markers of bone formation (Lucas, 2002; Brooks, 2004) or BMD (Dodin, 2005).

21.6 Cognitive function

21.6.1 Introduction

Cognitive function is the conjunct of intellectual abilities including memory, learning, perception, abstract reasoning, attention and judgement. In cognitive testing several domains are recognised. Subtle losses in cognitive function may be symptomatic of normal ageing or of a transition to early Alzheimer's disease (AD).

An important cognitive domain is memory, to be distinguished in verbal memory, visual memory and working memory: the ability to hold information in mind and manipulate it. Attention and concentration are a crucial part of all cognitive tests and therefore are also tested as a separate entity. Abstract reasoning and concept formation refer to the quality or process of thinking.

Mild cognitive impairment (MCI), as this state is most frequently termed, is defined as a slight impairment in cognitive function (typically memory) with otherwise normal function in the performance of activities of daily living. On the continuum of cognitive function, MCI lies between and overlaps normal aging and AD, and it is now recognised as a risk factor for AD, increasing the risk by a factor 4–5 (Levey, 2006).

Eventual outcomes associated with the various subtypes of MCI may include depression, vascular dementia, frontotemporal dementia, Lewy-body dementia, primary progressive aphasia, and Parkinson's disease. However, MCI also may remain stable or be reversed.

Evidence from population-based studies in older adults (age $\geq$60 or $\geq$65 years, depending on the study) suggests a prevalence of MCI in North America and Europe that ranges from 11% to 17% (Di Carlo, 2000; Ganguli, 2004;

Graham, 1997; Lopez, 2003; Ritchie, 2001), somewhat higher than the prevalence of dementia (6%–8% (Di Carlo, 2000; Graham, 1997; Lopez, 2003). Consistent with the use of various definitions and diagnostic criteria, reported rates of annual conversion from MCI to AD also vary substantially between 4% and 25% (Petersen, 1999; 2004; Ritchie, 2001; Devanand, 1997; Flicker, 1991; Tierney, 1996).

21.6.2 Isoflavones

Several animal studies suggested that isoflavones improve cognitive function in females, but not in males, especially in the memory domain (Pan, 2000; Lund, 2001). It is suggested that soy isoflavones act as oestrogen agonists, and therefore do not block beneficial effects of oestradiol (Lee, 2005). The first study in humans analysed data of the Honolulu-Asia Ageing Study (HAAS), an ongoing epidemiologic investigation that utilises the study population and data of the Honolulu Heart study. In this cohort study, assembled in 1965 among 8006 Japanese-American men aged 45–65 years, cognitive testing was done in 948 men and 502 spouses between 1991 and 1993. Diet was assessed in the males in 1965 and 1971, and a composite score for tofu consumption was constructed from these data. In this study, higher tofu consumption was associated with decreased performance on cognitive tests later in life (White, 2000). Soon after this study, a small randomised trial was published among male and female college students, who were randomised to a daily diet containing either 100 mg or 0.5 mg of isoflavones. In this study, the high-isoflavone diet resulted in significant improvements in verbal and non-verbal episodic memory, complex mental tasks, but not in attention (File, 2001). The study was not blinded with regard to the treatment. Subsequently, six randomised controlled trials on cognitive function effects of isoflavones have been reported in post-menopausal women. The studies differed in size from 2×25 in a cross-over study to 2×87 in a parallel group design, and in duration from 6 weeks to 12 months. The results are mixed and difficult to interpret. Some of these studies did find beneficial effects of the isoflavone treatment on memory tasks (Duffy, 2003; Kritz-Silverstein, 2003; Casini, 2006) some found a beneficial effect on attention (Duffy, 2003; Casini, 2006), and one on complex mental tasks (File, 2005), but two did not find any effects, among which the largest and with the longest duration (Howes, 2004; Kreijkamp-Kaspers, 2004b). Overall, these findings do not call for recommendations of increased isoflavone intake for protection against cognitive decline to postmenopausal women.

21.6.3 Lignans

In 2003 a paper was published which showed that of three strains of flax seed containing various amounts of lignans as well as alpha-linolenic acid, the variety with the highest content of lignans and the lowest amount of alpha-linolenic acid was associated with the least increase in peripheral resistance during stress, the

greatest reduction in plasma cortisol during stress and the smallest increase in plasma fibrinogen during mental stress in a Latin-square cross-over trial among 35 postmenopausal women (Spence, 2003). This finding might suggest a potential beneficial effect of lignans on cognitive function. Later, research from our group showed that higher dietary lignan intake was associated with better cognitive performance as measured with the Mini Mental State Examination, a screening questionnaire for dementia (Franco, 2005), and also with processing capacity and speed, and executive function (Kreijkamp-Kaspers *et al.*, 2007) in two cross-sectional studies among postmenopausal women. These findings call for further research into the role of lignans

21.7 Future trends

With respect to isoflavones, differences in metabolism have been proposed as a possible reason for sometimes finding an effect, and sometimes finding nothing. Metabolism is highly variable from person to person (Setchell *et al.*, 2003) and only one third of the population is capable of producing the isoflavone metabolite equol. This metabolite binds with the highest affinity to the oestrogen receptor, and only the producers of this metabolite may benefit from treatment (Setchell *et al.*, 2002). Also, genetic susceptibility might play a role (Hall, 2005; 2006).

If phytoestrogens do indeed exert their function through the oestrogen receptor, the endogenous hormone status could be an important modifier of the effects, complicating comparisons of findings in men and pre or postmenopausal women. For postmenopausal women, timing of the intervention might be important as the most successful trials were in peri or early postmenopausal women, suggesting that early supplementation to prevent changes related to the menopause might be effective while late intervention, to reverse changes that have already occurred, could be ineffective.

To conclusively answer the question whether isoflavones could improve health, at least for some groups of women, more clinical trials are needed. With respect to timing of exposure, sufficient numbers of recent and long post-menopausal women will have to be enrolled. Prior stratification for equol producers and non-producers would gain more insight in the effect of metabolism. For the exposure, it would be important to know the exact content of any supplement used. For inferences on the effect on bone, supplements should be given for rather long periods of time, at least one year, but preferably even longer.

Lignans are a less well studied class of phytoestrogens. Of course, a causal interpretation of the role of lignans is difficult from observational research. Confounding is a major concern in observational studies, in particular, high intake of lignans might be an indicator of some other important factor like a healthier lifestyle, or simply a better dietary pattern including more fruits and fibres. While the studies described before did adjust for many cardiovascular risk factors including lifestyle and dietary factors to minimise potential

confounding, this can never be ruled out completely. Very few trials have been performed using lignans.

A possible explanation for a greater vascular benefit of dietary lignans compared to isoflavones could be related to the Western dietary pattern. Sources of lignans, fruits and vegetables, tend to be consumed on a daily basis while sources of isoflavones, like soy, are more likely to be consumed on a weekly or even monthly basis. This might result in a more even exposure over time allowing lignans to exert a continuous effect while the isoflavones will result in an intermittent exposure.

Furthermore, the differences in the chemical structure of lignans compared to isoflavones, and thus the mechanism of action, might play a role. Little is known about the exact mechanism of action for both lignans and isoflavones. An important, and often overlooked difference between lignans and isoflavones is the binding to the oestrogen receptor. In contrast to what is often thought, the limited data available indicate that lignans do not bind to the oestrogen receptor (Saarinen, 2000), and thus their effects are probably mediated via other pathways (Kuiper, 1997; 1998). Lignans posses weakly oestrogenic and anti-oestrogenic activity and the protective effects of mammalian lignans may be due to their ability to induce sex hormone binding globulin (SHBG), to inhibit placental aromatase, and to act as antioxidants (Wang, 2002).

In conclusion, the promising findings with lignans in observational studies, combined with the disappointing results of recent trials with isoflavones warrant a shift of scientific attention and effort towards these 'forgotten' phytoestrogens, the lignans. For the time being, until new data becomes available, post-menopausal women should not be advised to use phytoestrogens supplements, until new data becomes available.

21.8 Sources of further information and advice

In 2005, the Tufts–New England Medical Center Evidence-based Practice Center (EPC) published an evidence report on the effects of soy on health outcomes (Balk, 2005).

In 2006, the NTP Center for the Evaluation of Risks to Human Reproduction (CERHR), established by the National Toxicology Program (NTP) and the National Institute of Environmental Health Sciences (NIEHS) recently published reports on the reproductive and developmental toxicity effects of genistein (Rozman, 2006a) and soy formula (Rozman, 2006b). These extensive reports provide the latest available evidence on the effects of soy isoflavones on cardiovascular disease and its risk factors, menopausal symptoms, cancers and their risk factors, bone health – osteoporosis and fracture risk, kidney disease, developmental and reproductive health.

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22

Food–drug interactions in older people

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Abstract: As a general rule, the use of medication increases considerably with advancing years. In many cases, the elderly are using drugs for chronic and degenerative disease for longer periods of time. Polypharmacy, the combined use of several drugs, is generally regarded as a high risk, especially in a population that is already at risk because of various other factors. Not surprisingly, adverse drug reactions are a major problem in elderly persons and a common cause of admission to hospital. Compared to drug–drug interactions, the possible effects of food on drug actions or side-effects or, *vice versa*, the effects of drug use on (micro-)nutrient status are receiving far less attention. Drug–nutrient interactions can be bi-directional. The vast majority of the literature concentrates on the general mechanisms of food effects on drugs. By contrast, much less is known on the effects of drugs on micronutrient uptake, storage or elimination. Effects of medication on nutrient status are easily overlooked, as they generally develop slowly and may go together with other social, nutritional, clinical and other changes. It seems conceivable that drug-induced nutrient deficiencies are relatively more frequent in the elderly than in younger patients. This chapter discusses the most important examples and mechanisms of drug–nutrient interactions. Attention is also paid to general age-related changes in drug effects. In the elderly, dietary habits may change, food intake tends to decrease and requirements of macro- and micronutrients may be different. The use of medicinal preparations, including OTC products and food supplements is on average very high in the elderly population. The sparse systematic information that is available on drug-induced changes in nutrient status, for example B12 and D, is often limited to studies in younger people and comprise one drug at a time. It seems highly conceivable that drug–nutrient interactions are under-diagnosed in the elderly population and that there may be much more under the water line. This will be particularly true for specific groups such as frail elderly persons taking several drugs at a time, or persons

having a low dietary intake. Health care professionals should be aware that an elderly person's new symptoms can be attributable to an underlying drug–nutrient interaction.

Key words: polypharmacy, medication, drug–nutrient interactions, nutrient depletion, micronutrients, OTC, food supplements, vitamin B12, folic acid, vitamin D.

22.1 Introduction

With advancing years, the use of medication increases considerably in the population. Rough estimates indicate that in Western countries the population of over 65 years uses between 30 and over 40% of all prescription drugs, while only representing between 10 and 15% of the population (McCabe, 2004; CBS Statistics Netherlands, 2007). In the Netherlands, people of 65 years and older consume three times as many medicines as the average Dutch person. For people aged 75 years and above, the consumption pattern even increases to almost four times the level of the average (SFK, 2007). Even more important than these total consumption figures is the high incidence of *polypharmacy* (the use of more drugs at the same time) in the elderly population. For example, figures for the US suggest that more than 40% of the non-institutionalised population aged 65 years or older uses five or more different medications per week (Gurwitz *et al*., 2003). In the Netherlands, the average senior citizen uses three different drugs simultaneously (SFK, 2007). This combined use of several drugs is generally regarded as a high risk, especially in a population that is already at risk because of various other factors. In addition to prescription drugs, the use of over-the-counter (OTC) preparations, complementary remedies and food supplements is reported to be high as well for the elderly population. Not surprisingly, adverse drug reactions (ADRs) are a major problem in elderly persons and a common cause of admission to hospital (Gurwitz *et al.*, 2003; Routledge *et al*., 2004; Hilmer *et al.*, 2007). Most adverse drug reactions in elderly persons can be classified as an 'accentuation' of the known pharmacological effects of the drug, and thus predictable and potentially avoidable (Routledge *et al.*, 2004). It is generally accepted that age-related physiological changes and drug–drug interactions are an important cause for this high frequency of ADRs (Mallet *et al.*, 2007; Becker *et al.*, 2007). On the other hand, drug–*nutrient* interactions are receiving far less attention. Drug–nutrient interactions can be bi-directional. The vast majority of literature concentrates on the general mechanisms of food effects on drugs. By contrast, much less has been published on effects of drugs on micronutrient uptake, storage or elimination. Although drug-induced nutrient deficiencies are regularly reported, there may be much more under the water line. One of the explanations is that these interactions are easily overlooked, as they generally develop slowly and may go together with other social, nutritional, clinical and other changes. It seems conceivable that drug-induced nutrient deficiencies are relatively more frequent in elderly than in younger patients.

Elderly persons may have specific nutritional requirements and nutrient deficiencies are already quite common in this group. This, together with the high incidence of polypharmacy, age-related physiological changes, and a potentially increasing vulnerability, underlines the importance of paying more attention to this topic.

22.2 Drug use in the elderly

Although elderly may use drugs of virtually all therapeutic classes, the high incidence of chronic and degenerative diseases in this group leads to an over representation of specific classes (Table 22.1). The following table provides a qualitative indication of drug classes that show a relatively high frequency of use in elderly persons (Bates *et al.*, 1999; Akamine *et al.*, 2007; SFK, 2007). It should be noted that some differences may exist between countries in this respect.

For example, in 2005, the most frequently prescribed drug in the Netherlands to elderly (over 65 years of age) was metoprolol (1.7 million prescriptions). The main indications for this medicine are hypertension and angina pectoris. Second was the antiplatelet agent acetylsalicylic acid (1.6 million prescriptions) followed by sleeping agent temazepam (1.4 million prescriptions). In shared fourth place were the antiplatelet agent calcium carbasalate (Ascal®) and the diuretic furosemide (both 1.3 million prescriptions) (SFK, 2007).

As already mentioned in the previous section, polypharmacy, the combined use of drugs, is a typical problem in elderly. There is no strict consensus on the definition for polypharmacy, but the term typically starts with situations in which four or more drugs are used for periods of over one month. Polypharmacy is almost non-existing in patients below the age of 30 years, but rises steadily to figures that can become quite dramatic in certain elderly populations (Hilmer *et al.*, 2007). Polypharmacy is particularly frequent in nursing homes. For example, in a recent publication Finkers *et al.* (2007) describe polypharmacy in five Dutch

Table 22.1 Some examples of drug classes that show a relatively high frequency of use in elderly persons

- Cardiovascular drugs (beta-blockers, ACE inhibitors)
- Lipid-lowering drugs
- Diuretics
- Antithrombotics (antiplatelet drugs and anticoagulants)
- Laxatives*
- Sedatives
- NSAIDs*
- Drugs against osteoporosis (in particular bisphosphonates)
- Drugs for benign prostate hypertrophy
- Antidiabetic drugs (for type 2 diabetes)

* including a large percentage of non-prescription (OTC) drugs.

nursing homes, with a total of 742 beds. For this study, the authors define polypharmacy as using more than *nine* drugs at the same time. The percentage of nursing home patients meeting the polypharmacy definition ranged from 14.6% to 19.8%. Drugs belonging to the classes 'alimentary tract and metabolism', 'cardiovascular system' and 'nervous system' were prescribed most frequently in the polypharmacy population. A discussion on the risks of polypharmacy *per se* falls outside the scope of this book. However, in relation to nutrition it is of importance to realise that polypharmacy is a significant problem in the elderly. The risk for drug–drug interaction goes up with the number of medications used. Indeed, drug–drug interactions account for a large percentage of ADRs in elderly. To what extent nutritional factors will further aggravate these complex interactions is left to speculation. However, it is highly conceivable that nutrient–drug interactions in various forms will pose an additional risk on top of the risks of drug–drug interactions. It is important to realise that the principles and examples of drug–nutrient interactions that are being described in the next sections are often derived from relatively simple 'one-to-one' situations. What about a frail elderly patient who is using eight drugs, and at the same time has a deficient diet?

22.3 Over-the-counter and herbal preparations

In addition to prescription drugs, elderly are frequent consumers of herbal preparations and/or food supplements (GAO report, 2001; Costello *et al.*, 2004; Canter and Ernst, 2004; Hilmer *et al.*, 2007). For example, according to the 2001 GAO report, it was estimated that 4 out of 10 elderly individuals in the US were using some type of herbal supplement. The general impression is that these figures are more likely to have increased than decreased since then. The regulatory framework under which herbal preparations are being regulated varies. In many countries, they fall under a nutrition regime. A number of preparations are specifically used by elderly to relieve problems associated with aging (GAO report 2001; Costello *et al.*, 2004). These include the so-called anti-aging health products such as dehydroepiandrosterone (DHEA) and other supplements such as *Ginkgo biloba*, ginseng, saw palmetto, St John's Wort and valerian. Herbal preparations and other food supplements are not by definition harmless. In addition, and in spite of a common belief, they may also give rise to various interactions with drugs (for example, Hu *et al.*, 2005; De Smet, 2007). Medical doctors and pharmacists are often not aware of the use of these preparations, and may also not always have enough knowledge on their potential risks, including the risk of causing interactions with 'regular' drugs.

Another group is formed by the non-prescription drugs (OTC). Elderly have been reported to consume relatively often NSAIDs (for pain relief), sedatives and H2 blockers (against gastric burns) (McCabe, 2004; Sawyer *et al.*, 2006). In addition, laxatives are relatively taken more by elderly, even when not constipated (Spinzi, 2007). Similar to food supplements and herbal products, the

use of non-prescription drugs is often not known to the medical professionals or the nursing staff. In some persons, a loss of memory can make the situation even worse. It is important that attention is paid to these groups of preparations, also in relation to the issue of nutrient–drug interactions.

22.4 Effects of nutrition on drugs: background and mechanisms

In principle, numerous interactions take place between nutrients and medications, but some interactions are more relevant than others. Nutrients and drugs (in particular with oral medication) share the same passage, absorption, transport and biotransformation processes. Metabolic pathways and mechanisms of effect are essentially similar: in principle, our body doesn't make any difference between 'drugs' and '(micro-)nutrients'. From a biological perspective this is easy to understand. Many drugs were originally derived from natural products, often secondary plant metabolites. Related compounds can still be present in our diet, although often in smaller amounts and in complicated mixtures. Macronutrients can also affect drug action. This can be acutely, for example by interfering with the passage through the GI tract or affecting absorption in a physical way. In addition, long term eating behaviour, for example leading to obesity, or fasting, etc., can have implications for the action of drugs. As a general rule, most effects of nutrients on a patient's response to drugs are *pharmacokinetic effects.* In pharmacology, the pharmacokinetic phase refers to the processes of drug absorption, distribution, metabolism and excretion (ADME). Effects of nutrition on the *pharmacodynamics*, i.e. the processes of interaction between the active drug molecules and biological structures or processes, are seen less frequently.

As an overview, Fig. 22.1 shows the general processes that take place after a drug enters the body and some possible sites of interaction with food. From the basic principle that nutrients and drugs share the same physiological pathways, it may be concluded that there may always be some form of interaction taking place. Fortunately, most of these interactions remain unnoticed or are not clinically relevant. To have an effect on the activity (effect or side-effect) of a drug, the following general rules apply for a nutrient or mixture of nutrients:

- The nutrient(s) directly or indirectly affect(s) one or more rate-limiting step(s) of the pharmacokinetics of the drug, or the nutrient(s) compete(s) with the drug for an enzyme, receptor or transporter that has a direct effect of the pharmacodynamics of the drug.
- There is a close relation between the response of the body and these process(es).

In relation to the second issue, it is relevant to understand the principle of the *therapeutic window* or *therapeutic ratio* of the drug. These terms are used to define the difference between the effective dose (or plasma concentration) and

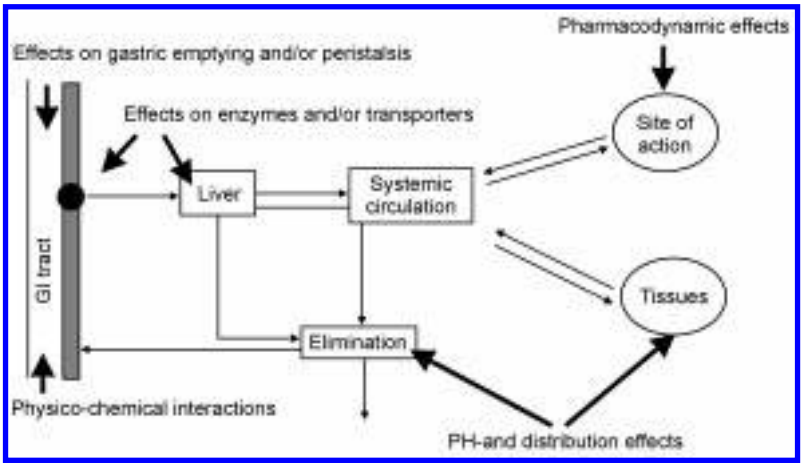

Fig. 22.1 Schematic overview of the processes after a drug enters the body and the most common sites of interaction with food.

the toxic dose (or plasma concentration). Some drugs, for example many (but certainly not all) antibiotics, are relatively non-toxic. When a food component causes an increased plasma concentration of that drug, this effect will often not be clinically relevant. In some cases, however, for example with immunosuppressant or cytotoxic drugs, the difference between an active and toxic plasma concentration is small. A small increase or decrease of that concentration induced by food may have dramatic consequences.

22.4.1 Pharmacokinetic effects of nutrients on drugs

Most of the acute and sub-acute interactions between food or nutrients and drugs belong to one of the following categories:

- Interactions in the GI tract.
- Interactions at the level of drug absorption.
- Interactions at the level of drug biotransformation.

In addition to these (sub-)acute and mostly direct interactions, dietary habits, lifestyle and other long-term consequences of the diet may have pharmacokinetic consequences. However, there is relatively little systematic knowledge on, for example, the effects of obesity or chronic malnutrition on the pharmacokinetics of drugs. Depending on the nature of the drug, obesity may require dose-adjustment (Cheymol, 2000). Chronic malnutrition resulting in hypoalbuminemia may change the pharmacokinetics of drugs that are tightly bound to plasma proteins (Lindow and Wijdicks, 1994).

Interactions taking place before drug administration

Although the focus of this chapter is on drug–nutrient interactions that occur in the body, interactions taking place *before* the drugs and food are taken might

become relevant in specific groups. In case persons have problems with eating or swallowing or have other physical obstacles, drugs may be mixed with food or drinks. In patients that receive enteral tube feeding, drugs are also often mixed with the food.

Various chemical or physical interactions can take place in these situations. Some of the principles (i.e. complexation) are similar to those that may occur in the GI tract, which will be discussed in the next section. In addition, certain preparations such as controlled release tablets may not be broken or crushed in order to mix them with food or drinks. Those formulations are, for example, designed to release the drug over a certain period of time and breaking could result in the release of the total amount at once. As a general rule, mixing drugs with food should never be done without verifying that this is possible. Nowadays, practical guidance and formularia for common drug preparations are (or should be) available in most hospitals and nursing homes.

Interactions in the GI tract

One type of drug–nutrient interaction is a direct chemical interaction between a drug and a food component, known as a complexation or chelation reaction, which produces a complex that can not be absorbed from the GI tract. The combination of tetracycline with divalent cations, such as the calcium in milk, dairy products or antacids, is an example of a chelation reaction. Complexation reactions can also occur when iron (ferrous or ferric salts) binds with tetracycline or with fluoroquinolone antibacterials (for example, ciprofloxacin or norfloxacin). The combination of zinc plus fluoroquinolones may result in an inactive complexation or, by a separate non-specific effect, in decreased absorptive capacity. Calcium may also have an adverse effect on the absorption of quinolones. The effect of dairy products is well known in this respect. Most physicians and pharmacists are indeed now trained to inform the patient, and drug information leaflets are mentioning this risk. However, far less attention is being paid to similar and probably even larger effects of ions in food supplements and OTC products. Therefore, it is important to advise patients to avoid concomitant ingestion of calcium-containing food supplements, enriched food products and over-the-counter products (e.g., vitamins containing iron, zinc or magnesium and antacids containing calcium) when taking these groups of antimicrobials. If patients must take the combinations outlined above, an interval of at least two hours is recommended. Treatment with tetracycline or quinolone antibacterials will mostly have a temporally character, and is not a specific issue for the elderly population. A chemically similar phenomenon is seen between calcium and bisphosphonates which are often (but not exclusively) used to treat osteoporosis in post-menopausal women. Examples include alendronate and risedronate which can form stable complexes with calcium ions. If this occurs in the GI tract, absorption can be completely inhibited. Therefore, patients are not allowed to eat or drink anything that may contain Ca or other divalent cations for a period of one to several hours before or after taking the drug. For many persons this is particularly uncomfortable as nausea is a common side-effect of

bisphosphonates. Fortunately, new formulations and treatment schedules have become available allowing the drug to be taken once weekly instead of daily. There are some reports on an interaction between dietary fibres and drugs (e.g., digoxin and some, but not all, statins) caused by binding of the drug to the fibres.

Effects of gastric emptying rate

Delayed emptying may slow down the rate of drug absorption. The total amount (finally) absorbed may differ and depends amongst others on acid stability and dissolution rate. A number of antibiotics (for example, many penicillins or macrolides) show high susceptibility to gastric inactivation. Taken with food, their bio-availability can be reduced by decreasing the gastric emptying rate and prolonging exposure time to breakdown by gastric acid. On the other hand, there are also examples of drugs (for example, the antifungal drug itraconazole) that benefit from a longer residence in the stomach. This is at least in some cases caused by a better environment for dissolution (mixing and low pH). Many drug–nutrient interactions delay the absorption rate of the drug without significantly affecting the extent of the drug absorption. While these drug–nutrient interactions usually do not result in therapeutic failure, patients should be advised to take their medicine in a consistent relationship to meals and, in most situations, on an empty stomach.

Effects of fat

Dietary fat may affect the absorption of certain drugs. However, the extent and direction of the effects can vary. With reference to the previous paragraph, it is well known that fat can slow down gastric emptying rate, resulting in at least a slower absorption. However, fatty meals can increase the amount of drug absorbed from the GI tract. This is not only the case with certain lipid-soluble vitamins, but also with their 'drug' derivatives such as isotretinoin. Fat can also reduce the absorption of certain drugs. An example is the immunosuppressant drug tacrolimus. Food has also been shown to increase the bioavailability of an oral solution of cyclosporine, another immunosuppressant drug. Because of the variation of effect of fat and the difficulty to predict the direction, the most practical advice is to keep the fat percentage of the diet as constant as possible. This might particularly be relevant for those persons that are daily receiving a cocktail of drugs. In relation to this it is also advisable to pay attention to incidental changes in the diet, when unexpected reactions to drugs are seen. This may, for example, become manifest in a person who normally takes very small meals.

Effect of nutrients on 'drug' transporters

During the last decades it has become clear that many bio-active molecules are taken up from the GI tract via active transporters. This transcellular transport of many chemicals, food ingredients, drugs or toxic compounds over the intestinal epithelium can be highly dependent on the activity of membrane bound ATP binding cassette (ABC) transport proteins (Brand *et al.*, 2006 for review). Many

of these transport proteins are not only important for the transport of drugs and nutrients itself, but their activity can also be affected by compounds present in the gut lumen. For example, many flavonoids are known for their inhibition of ABC transporters. By doing so, they may affect the bioavailability of drugs, bioactive food ingredients and/or food-borne toxic compounds upon oral uptake. Although there are more and more papers describing the effect of flavonoids *in vitro* or in experimental animals, data obtained in humans are relatively scarce. An additional difficulty is that flavonoids are usually present in mixtures and subject to metabolism inside the GI lumen. An interesting example is given by Dresser *et al.* (2002) who showed that ingestion of grapefruit, orange and apple juice caused a decrease in the absorption of the antihistaminic drug fexofenadine, resulting in unexpectedly low blood levels. Clinically, this is also a remarkable observation. As will be discussed in the next section, grapefruit juice is mostly known to *increase* blood levels of several drugs. This is due to an inhibition of certain cytochrome P450 (CYP450) enzymes by flavonoids present in the fruit. Later, the same group showed that the flavonoid naringin is responsible for this highly selective effect on the intestinal transporter protein (Bailey *et al.*, 2007). Another interesting observation from the first study (Dresser *et al.*, 2002) was that in this case, orange juice and apple juice caused a similar effect as grapefruit. In contrast to grapefruit, orange and apple juice are not known for their CYP450 inhibiting properties and are generally considered as 'safe' when it comes to nutrient–drug interactions. As these fruits don't contain significant amounts of naringin, other compounds will probably be responsible for this effect. This example clearly illustrates that interactions between flavonoids in the diet and drugs via ABC transporters can be very specific and may occur rather unexpectedly. It is conceivable that there may be more of these unpleasant surprises below the waterline, underlining the importance of good observation in clinical practice. Of special interest in this respect are herbal preparations and certain teas, which may contain high levels of flavonoids.

Effects of nutrients on biotransformation

Interactions between nutrients and drugs at the level of biotransformation are probably the most important class. Not only are many interactions known, with most likely many more to be discovered, but the majority of the clinically severe cases that are known to date fall into this category. Of particular interest are the effects of nutrients on cytochrome P450 (CYP450) enzymes, which are still causing a number of lethal interactions each year. Much of the CYP450 is found in the liver, the main organ involved in drug metabolism. A substantial amount is also found in the small intestine. CYP is located in the 'microsomal' part of the cytoplasm (endoplasmic reticulum). CYP450 is vital to the formation of cholesterol, steroids and arachidonic acid metabolites. In addition to these endogenous molecules, CYP450 enzymes are the most important enzymes that catalyse the oxidation of many drugs and other molecules including plant metabolites and environmental contaminants, that we are exposed to. Although

the process is called oxidation, the reactions that are seen include N-dealkylations, O-dealkylations, hydroxylations as well as epoxidations and S-oxidations. CYP450 is called a '*superfamily*' of enzymes (Nelson *et al.*, 1996). This superfamily is further divided into families (for example CYP1, CYP2, etc.) and subfamilies (for example CYP1A, CYP1B, etc.). In humans, more than 50 individual enzymes have been identified to date. These are mostly called *isoforms* and show a certain (but sometimes overlapping) substrate specificity. This means that the main biotransformation reactions for specific drugs are preferably catalysed by this enzyme. Seven of the isoforms are responsible for the major part of the biotransformation of drugs that are currently in use. Examples are given in Table 22.2.

Table 22.2 Examples of CYP 450 enzymes, together with some preferred substrates, inhibiting or inducing drugs or foods

Subfamily	Enzymes	Examples of substrates	Examples of inhibitors	Examples of inducers
CYP1A	CYP1A2	Caffeine, Theophylline	Certain quinolone antibiotics, Fluvoxamine	Broccoli, Brussels sprouts, Charcoal
CYP2C	CYP2C9	Many nonsteroidal anti-inflammatory drugs, Phenytoin, S-warfarin	Fluconazole, Metronidazole, Amiodarone	Rifampicin
	CYP2C19	Omeprazole and other proton pump inhibitors, S-mephenytoin	Cranberry, Fluoxetine	
CYP2D	CYP2D6	Several beta blockers, Amitriptylline and other antidepressants, Haloperidol	Quinine and Quinidine	
CYP2E	CYP2E1	Several anesthetics, chlorzoxazone, Ethanol	Garlic, Cabbage	Ethanol
CYP3A	CYP3A4	Several macrolide antibiotics, benzodiazepines, Cyclosporine, Tacrolimus, several HIV antivirals, Calcium channel blockers, Statins, Steroids and many more compounds	Grapefruit, Star fruit, Wine, Ketoconazole, HIV antivirals	St John's Wort, Dexamethasone, Phenobarbital

More extensive tables, including tables with interactions, are available via the Internet. A very useful link is the 'Dave Flockhart' table, maintained and regularly updated by the division of Clinical Pharmacology of Indiana University School of Medicine (*http://medicine.iupui.edu/flockhart/table.htm*). Cytochrome P450 mediated metabolism rates vary among persons. Part of this can be explained by *genetic polymorphism*. This may lead to so-called 'poor' or 'extensive' metabolisers. Some patients metabolise a drug so rapidly that therapeutically effective blood and tissue concentrations are not reached. In others, metabolism may be so slow that usual doses have toxic effects. CYP450 is affected by many other factors such as disease, age and gender. For example, with aging, the liver's capacity for metabolism through the cytochrome P-450 enzyme system is reduced by $\geq$30% (see Section 22.3). In many cases, only specific enzymes are affected. As a consequence, it depends on the biotransformation route of that drug whether or not this is therapeutically relevant. In relation to interactions, it is important that CYP450 enzymes can be induced or inhibited by other drugs and dietary components. The first category is nowadays receiving considerable attention. Potential drug–drug interactions are already investigated before registration and computer systems at pharmacies give warning signals for potential interactions. Effects of nutrients on CYP450 are known as well. Some effects (such as grapefruit juice, and possibly cranberry juice) are very potent and comparable to those of drugs. Others are less strong and sometimes questionable. Therefore, it is difficult to say whether this phenomenon is under- or overestimated. On the one hand there are many examples known in which individual nutrients or small mixtures have been found to inhibit certain CYP450 enzymes *in vitro* or in experimental animals. On the other hand, the number of well-documented clinically relevant cases is limited. Complicating factors include the standardisation of the food, for example in terms of flavonoids present, the effect of mixtures, individual or genetic differences, etc. It is also clear that these studies are quite costly and that financial sponsors are difficult to find. The elderly population may be at particular risk here, considering the high incidence of polypharmacy, the decrease in CYP450 capacity and possible dietary complications in general. Some examples will be discussed below.

The effect of cranberry juice on CYP2C9

Cranberry juice and supplements containing cranberry extract have become a popular remedy for treatment or prevention of urinary tract infections also in elderly persons. Several case reports suggest that cranberry can cause serious interactions with certain CYP450 enzymes, in particular CYP2C9. This enzyme is amongst others involved in the metabolism of the anti-thrombotic drug warfarin. Several case reports have been published describing this interaction. For example, Suvarna *et al*. (2003) describe an interaction in a 70-year-old man who died of massive bleeding which was attributed to such an interaction. Another example of a serious internal bleeding is described by Rindone and Murphy (2006). However, it should be mentioned that the interaction with

cranberry has also been questioned. Some intervention studies failed to demonstrate any effect (see review by Pham and Pham, 2007).

Effects of grapefruit juice (and other foods and drinks) on CYP3A4
The effect of grapefruit juice on the biotransformation by CYP450 is by far the best known example of a food (drink)–drug interaction. Indeed, hundreds of papers have been published on this subject (Aronson, 2001; Huang and Lesko, 2004). Due to an inhibition of CYP4503A4, the biotransformation of compounds that are predominantly metabolised by this enzyme is decreased. This has caused several clinically relevant interactions, for example with cyclosporine, atorvastatin, simvastatin, felodipine, terfenadine, saquinavir, midazolam and triazolam.

Effects of St John's wort (Hypericum perforatum)
St John's wort is a popular herbal preparation used for its antidepressant activity. In most countries it is regulated as a food supplement. Chronic (two week) administration of St John's wort can result in an *induction* of CYP3A4 (Huang and Lesko, 2004). This has, for example, resulted in a warning for low-dose contraceptives where more breakthrough bleedings were observed.

Other foods or preparations that have been implicated in interactions at the level of CYP450 include star fruit (inhibition of CYP3A4), wine (*idem*), garlic (inhibition of CYP2E), cabbage (*idem*), broccoli (induction of CYP1A) and roasted meat/barbecue meals (*idem*). Clinical relevance is not always clear.

Nutritional status in general
Severe malnutrition can result in hypoalbuminemia. In patients receiving drugs that are for a large percentage (>90%) bound to plasma proteins this might lead to an increase in the free fraction of the drug. For example, Lindow and Wijdicks (1994) describe a case of an 80-year-old woman who had increased phenytoin (an anti-epileptic drug) blood levels due to hypoalbuminemia. This caused (reversible) symptoms of intoxication.

22.4.2 Pharmacodynamic interactions

The majority of drug–nutrient interactions that are known belong to the pharmacokinetic interactions. Compared to this, pharmacodynamic interactions seem to appear far less, although some may be not recognised as such. A few examples include:

- Vitamin K and coumarins
- MAO inhibitors and tyramine
- ACE inhibitors and K+
- Pyridoxine and levodopa
- Alcohol and CNS drugs.

Patients using coumarins (acenocoumarol, fenprocoumon, warfarin) for anticoagulation therapy may be sensitive to dietary fluctuations of foods high in

vitamin K. This is understandable, as coumarin derivatives act as vitamin K antagonists. Foods known to be rich in vitamin K include green leafy vegetables (spinach, broccoli, Brussels sprouts), cauliflower, chick peas, green tea, pork liver and beef liver. For example, frequent intake of seasonal green vegetables can add to the total body stores of vitamin K, increasing the production of vitamin K dependent clotting factors. This may cause antagonism of warfarin and results in decreased therapeutic efficacy of the intended anticoagulation therapy (Singh, 1999).

Monoamine oxidase (MAO) inhibitors were first-choice antidepressant drugs in the 60s. Later, they lost their position to tricyclic antidepressants and SSRIs, also because of the acute hypertensive reactions following the ingestion of certain foods and beverages. However, for people with treatment-resistant depression they are still in use. MAO inhibitors are well-known for their interaction with tyramine. This may lead to a life-threatening hypertensive crisis. Unsafe foods include those high in protein that have undergone aging and/or fermenting (cheese), pickling (fish), smoking or bacterial contamination. Red wine, some types of beer (including non-alcoholic beer), fermented products (sausage), brewer's yeast and fava beans can also cause problems (McCabe, 2003). Dietary restrictions should continue for three weeks after discontinuation of the drug.

ACE inhibitors and potassium supplementation, for example in salt replacers, can lead to a life-threatening hyperkalaemia (Ray *et al*., 1999). Large doses (usually as supplements) of pyridoxine (vit B6) can reduce the effect of levodopa (used in Parkinson's disease).

22.4.3 Drug effects on nutritional status

There is considerably more knowledge on the effects of food or nutritional status on drug activity than *vice versa*. However, it is obvious that drug treatment, in particular chronic use, can lead to depletion of certain micronutrients. In addition, certain drugs can effect nutritional status in an indirect way, via a loss of taste or smell or an effect on appetite. Situations in which a drug interferes with nutritional status are frequently overlooked or diagnosed late (McCabe, 2004). This may be particular true for the elderly, in which nutritional status may already be less optimal and requirements higher.

Effects of drugs on taste or smell

Several drugs have been reported to affect taste or smell (Doty and Bromley, 2004 for review). As a gradual loss of taste and smell perception is also part of a physiological aging process, additional drug-induced effects may often be overlooked. However, it is obvious that a drug-induced disturbance of taste and/or smell leading to lower appetite and food intake in elderly may even be more disadvantageous than in younger persons. A drug can affect taste or smell in a direct way when it has a certain taste itself or inhibits or induces distortion of taste/odorant receptor function. Indirect effects include a change in

oropharyngeal microflora which may occur during antibiotic use. Another example is the reduction of cellular turnover in the nose epithelium or oral cavity due to cytotoxic agents (for example, anti-cancer). Many drugs have a bitter taste which can directly affect enjoyment of food. It is important to realise that bitterness, other bad taste perceptions, or indirect effects do not only occur after oral administration. With the antibacterial drug clindamycine, for example, a bitter taste is also reported after intravenous administration, due to the distribution to the saliva (de Groot and van Puijenbroek, 2007). The group of the angiotensin converting enzyme (ACE) inhibitors (captopril, enelapril, perindopril, etc.) are well known to cause the taste disturbances. A similar effect has been reported for angiotensin II receptor blocking drugs such as valsartan (Tsuruoka *et al*., 2005).

As loss of taste or smell can result from different factors, it is not always recognised as an effect of a drug. This becomes even more difficult when combinations of drugs are taken.

Effects of drugs on appetite

Next to the perception of food, drugs can also influence appetite and satiety processes. Again, these effects may be overlooked, for example when a person already has a low dietary intake or when social or emotional problems are involved. Interaction with appetite is typical for drugs acting on the central nervous system (CNS). Antidepressants of the SSRI (specific serotonin re-uptake inhibitor) class such as fluoxetine and citalopram often show anorectic effects and cause weight loss. On the other hand, patients taking antidepressants like mirtazepine and the tricyclic antidepressants often increase in weight. Benzodiazepines (for example, temazepam), as sedative or anxiolytic drugs frequently used by elderly, may cause a temporary increase in appetite. Other classes of CNS drugs (antipsychotics, anti-epileptic drugs, etc.) also regularly affect appetite.

A more non-specific but still relevant effect is the development of nausea. Again, when a person is already a ‘poor eater’, any additional reduction of appetite due to nausea may be extra harmful. For example, cholinesterase inhibitors which may have some benefit in (vascular) Alzheimer’s disease may lead to nausea and anorexia (Kavirajan and Schneider, 2007).

Effects of drugs on micronutrients

Medication can alter vitamin absorption, storage and metabolism. There are many reports describing drug-induced vitamin deficiencies. However, for some drugs and vitamins there is also considerable debate about the clinical significance and the need to administer extra vitamins. It is obvious that elderly who may already be at risk of vitamin deficiencies are an extra vulnerable group. Some examples:

- Vitamin B12 is among the vitamins that appear to be the most frequently depleted by drugs (McCabe *et al*., 2003). Several anti-epileptic drugs

(phenytoin, carbamazepin, phenobarbital, primidone and valproic acid), H2-blockers (cimetidine, ranitidine) and proton pump inhibitors (omeprazole and others) and the anti-diabetic drug metformin cause depletion or decrease absorption.

- Folic acid. Anti-epileptic drugs can cause folate deficiency. However, folic acid supplementation can reduce the plasma levels of the anti-epileptic drug and seizure control. Sulfasalazine (used in colitis) can reduce folic acid absorption.
- Vitamin D. Anti-epileptic drugs may cause an increased risk of osteoporosis and fracture. This may be caused at least in part by induction of cytochrome P450 and other enzymes leading to an increased catabolism of vitamin D. Low calcium intake and vitamin D deficiency may aggravate these bone effects and are potentially treatable factors. Inactivity is another risk factor (Valsamis *et al.*, 2006).
- Chronic use of laxatives containing paraffin reduces the absorption of fat-soluble vitamins. Other laxatives (bisacodyl and also the plant-derived preparations such as Senna en Rheum) are more related to reduced absorption of potassium.

Minerals, such as potassium and magnesium, can also be influenced by drug use. Potassium levels may require special attention. Diuretics are frequently used in the elderly population. Furosemide and thiazide diuretics can cause a loss of potassium (and magnesium as well). However, if patients switch to potassium sparing diuretics (amiloride, spironolactone, triamterene) there is a risk of developing hyperkalaemia. Elderly people may be relatively sensitive to developing hyperkalaemia (Butler and Hasan, 2002). High levels of potassium have also caused problems in situations where people using potassium-sparing diuretics and digoxin started using 'salt-replacers', which can contain K in stead of Na. Classical (almost lethal) interactions of this kind in elderly persons were described by Yap *et al.* (1976).

Effects of drugs on body water

Dehydration can occur rapidly in elderly persons with potentially severe effects. Acute dehydration may result from diuretic use, in particular with loop diuretics (Furosemide).

Prolonged use of certain laxatives (for example, bisacodyl) may result in a more gradual dehydration. Bulk-forming (for example, fibres) and osmotic laxatives (lactulose) require water to work. If fluid intake is insufficient the effect may be disappointing resulting in a desire to further increase the dose of the laxative. Polypharmacy has also been shown to heighten risk for dehydration. Lavizzo-Mourey *et al.* (1988) found a significant relationship between the use of more than four medications and severe dehydration in nursing home residents.

22.5 Age-related physiological changes relevant for pharmacology

Pharmacokinetics and pharmacodynamics may be altered in the aging population (Turnheim, 2003; Cusack, 2004; Mangoni and Jackson, 2004). This is due to normally occurring age-related physiological changes. However, large inter-individual differences exist in the speed of progress of these processes. This, and existing disease processes, frailty, stress and poor nutrition may overshadow age-related changes. The absorption rate of bio-active substances is generally not changing with aging (Cusack, 2004). The effect of aging on small-bowel transporter systems is not yet fully established. Bioavailability of highly extracted drugs is often increased with age. Relative decrease in total body water and increase in body fat may affect the volume of distribution. Fat-soluble drugs may distribute more widely and water-soluble drugs less extensively in older persons. As a result, half-life of fat-soluble drugs might increase and serum levels of water-soluble drugs might go up (lithium, aminoglycosides, digoxin). Again, inter-individual differences in body composition also make these factors variable among different persons.

In the liver a rather non-specific decrease in CYP450 activity occurs with aging. This generally leads to an age-related decline in the elimination of metabolised drugs. On top of this, frailty, physiological stress, and illness may further inhibit oxidative metabolism of foreign and endogenous compounds. The relative inhibition of drug metabolism by other compounds does not seem to be altered with aging, but some studies suggest that the process of enzyme induction might be reduced (Cusack, 2004). Phase-II metabolism (drug conjugation) is less affected by age. Other factors affecting hepatic elimination include a decline in liver size and blood flow. GFR is often going down but again highly variable. Creatinine clearance has been suggested not to be a reliable parameter to predict this (Hilmer *et al.*, 2007). Elderly patients generally show an increased pharmacodynamic response to several commonly used drugs, in particular those affecting the cardiovascular and central nervous systems (Turnheim, 2003; Mangoni and Jackson, 2004). It is also suggested that aging itself is associated with increased risk of adverse reactions to specific classes of drugs, for example NSAIDs, independent of polypharmacy and altered pharmacology (Hilmer *et al.*, 2007).

It is not easy to predict what the consequences of these age-related changes in pharmacology will be for drug–nutrient interactions. Only some general conclusions can be made. Pharmacologically speaking, the balance between drug effect and toxicity in elderly persons is becoming less stable. Relatively small differences in the diet may have more consequences for the effect of drugs than seen in younger persons. *Vice versa*, effects of drugs on micronutrient status may be much larger in older persons, who may already have a lower intake and/or increased need. This problem becomes ever more relevant but also more complex in frail elderly persons that may take several drugs together.

22.6 Conclusions

Drug–nutrient interactions should be considered as an issue of high clinical relevance for the elderly population. As described in the previous sections, and also in other chapters of this book, the main reasons for this are three-fold. First, drugs may have different effects and side-effects in older people. This is due to normal age-related changes in physiological functions and body composition that are taking place. Second, dietary habits may change, food intake tends to decrease and requirements of macro- and micronutrients may be different. Third, the use of medicinal preparations, including OTC products and food supplements is on average very high in the elderly population.

It seems highly conceivable that drug–nutrient interactions are underdiagnosed in the elderly population and that there may be much more under the water line. This will be particularly true for specific groups such as frail elderly persons, taking several drugs at a time, and having a low dietary intake.

Health care professionals might not suspect that an elderly person's new symptoms are attributable to an underlying drug–nutrient interaction. Although situations can be very different, the following general recommendations can be made:

- A person's diet and food and fluid consumption pattern should be taken into account when judging the clinical situation or the reaction to new or existing drugs.
- Older people should be encouraged to report the use of OTC products, herbs, vitamins and other nutritional supplements to their doctor or pharmacist.
- It is advisable to identify persons at risk for nutrient–drug interactions. For example: persons using multiple drugs, persons with low dietary or fluid intake, frail elderly, people suffering from depression or cognitive impairment, persons living alone, changes in the living environment.
- Define risky situations and keep record of these. This includes drug classes of particular relevance (diuretics, ACE inhibitors, CNS drugs, digoxin).
- Health care professionals and nursing staff should be aware of side-effects and drug induced nutrient deficiencies: mouth, dental, bleedings, falls, dizziness.
- A change in patients feeling, etc., should be considered as potential side effect.
- Consider a change in appetite, dietary or fluid intake as potentially drug related.
- Don't change too much in diet (especially not in fat content, fibres, etc.) when a person is using medicines.
- When a drug label states that there is no interaction with food, this is no guarantee. The FDA and other guidelines recommended diet to study food–drug interactions are high in fat and energy and low in nutrients (minerals and vitamins). This implicates that some drugs which are indicated 'as safe with food' may present side-effects in elderly patients or any other patients receiving multiple drugs and special foods. Examples include special diets in general, energy rich food and products for enteral feeding.

- Consider regular plasma analysis of vitamins (in particular B12, B6 and folate), minerals (K^+ and Mg^{2+}) and drugs in vulnerable patients. Attention should also be paid to fluid balance.

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23

Dietary supplement use in the elderly: benefits and risks

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Abstract: The advent of dietary supplements has meant that individuals do not need to rely solely on foods to provide the essential nutrients for health. This chapter discusses international trends in the use of dietary supplements in Western countries and, in particular, the characteristics and motivations of elderly users of supplements. It discusses the types of supplements consumed by older people and the circumstances where nutrient supplementation is beneficial to the health of the elderly, e.g. to maintain bone health or boost immune function. Finally, it addresses potential problems associated with excessive supplement use.

Key words: aged, elderly, dietary supplements, vitamins, minerals.

23.1 Introduction

Since the beginning of time humans have been able to obtain all the nutrients necessary to sustain life by eating a variety of foods. For almost our entire evolutionary history food alone provided these nutrients. However, advances in food technology have resulted in new and novel ways in which humans can meet their nutritional requirements. The advent of the dietary supplement has meant that it is no longer necessary for individuals to rely solely on foods to provide the essential nutrients for health. The widespread, global popularity of these products suggests that a significant portion of the population believe in the added value of supplemental nutrients, and consider these preparations as an appropriate way to meet their dietary and health needs. In relation to dietary supplement use in the elderly, this chapter will examine prevalence of

use in Western countries; characteristics of users; types of preparations consumed; reasons for supplement use; circumstances when supplementation is indicated and potential problems associated with supplement use in this age group.

23.2 International trends

Dietary supplements form an integral component of the health care strategies adopted by people throughout the world. Consumer expenditure figures on vitamin and mineral preparations, and population estimates of supplement use are evidence of a global trend towards individuals actively participating in decisions about their health and the medicines they use.

In the year ended 2005, sales for vitamins and dietary supplements in Australia reached AUD 907 million and grew 7% in current value terms compared to the previous year. In the United Kingdom and the United States, sales for these products reached £442 million and US$14,597 million respectively, over a similar period. In Europe, sales of vitamins and dietary supplements have also risen steadily. France, Germany and even Turkey have shown consistent growth in this sector of over-the-counter health care expenditure (http://www.euromonitor.com/OTC_healthcare).

23.3 Prevalence of supplement use

An accurate assessment of the extent to which the public use these products is confounded by the wide variation in the criteria used to define what constitutes a supplement (preparations including vitamins, minerals, herbals, others); different frequencies of use (regularly, irregularly) and different time frames during which supplement practice has been examined (day before interview, day of interview, past week, past month, past year).

Several countries have conducted utilisation studies; however, the majority of the information on this topic relates to the population of the United States. Since the 1970s numerous large-scale health and nutrition surveys conducted in the US have measured the prevalence of supplement use. A range of poorly defined expressions appear in the literature in reference to supplement use, such as vitamin and mineral supplements, dietary supplements, nutritional supplements, and food supplements (Dorant *et al.*, 1993; Eisenberg *et al.*, 1993; Ervin *et al.*, 1999). Often these terms are used in a seemingly interchangeable fashion and refer to an assortment of preparations including single vitamins, single minerals, mixed vitamin and minerals, yeast, kelp, garlic, bee pollen, ginseng, sports drinks, amino acids, lecithin and even injectable vitamin B12 (Brownie and Myers, 2004). Accepted definitions for these terms have only relatively recently been formalised in different countries.

In the US, Congress endorsed an official definition of the term dietary supplement, under the 1994 Dietary Supplement Health and Education Act, as 'a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients – a vitamin, mineral, amino acid, herb or other botanical' (NIH, 2003). In the UK, the term 'food supplement' is the preferred expression and has been defined under the Food Supplements (England) Regulations 2003 as 'any food for the purpose of which is to supplement the normal diet and which is a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination and is sold in dose form'. Australia on the other hand, refers to preparations that contain vitamins, minerals, herbals and other natural ingredients as complementary medicines, which also includes essential oils, homoeopathic preparations, and plant or herbal materials (TGA, 1999).

Depending on the population studied and the method of data collection used, 40–60% of the older age group regularly use some form of 'supplement' (Freeman *et al.*, 1998; Houston *et al.*, 1998; Vitolins *et al.*, 2000; Brownie and Rolfe, 2005). Several studies confirm that older people (i.e. aged 60–65 years and over) report higher rates of supplement usage than the general adult population (Koplan *et al.*, 1986; Subar and Block, 1990; Ervin *et al.*, 1999; Radimer *et al.*, 2004) (see Table 23.1). The highest estimate of regular supplement use by older individuals was reported in the fourth National Health and Nutrition Examination Survey, which found that 63% of individuals aged 60 years and over had used at least one dietary supplement during the previous month (Radimer *et al.*, 2004).

Table 23.1 Prevalence of supplement use by participants aged 60–65 years and over

Period prior to interview	First author	Age years	% who used supplements
At the time of investigation	Brownie	65+	43
	Freeman	60+	60
	Hale	65+	39
	Houston	60+	44
	Looker	65+	40
	Stewart	65+	42
During the week prior to investigation	Hartz	60+	50
During the two weeks prior to investigation	Bender	65+	40
During the month prior to investigation	Ervin	60+	47
	Horwath	65+	40
	Schneider	60+	45
	Vitolins	70+	47
	Radimer	60+	63

23.4 Characteristics of older supplement users

It is well established that supplement use in the older age group is positively associated with gender, ethnicity, level of education and nutrient intake, and to a lesser extent cigarette use. Some chronic health conditions act as impediments to supplement use in this age group.

23.4.1 Gender

In a review of the characteristics of older supplement users, Brownie (2005) found that gender was the most predictive determinant of supplement use both among the general and older adult population. This review found that women aged 60–65 years and over used dietary supplements including vitamins, minerals and herbal medicines, with significantly greater frequency than did men of the same age group in the majority of investigations.

In reporting on supplement practices in the early 1980s, Worsley and Crawford (1984) and Schneider and Nordlund (1983) both offered explanations for the higher use of supplements by women. Worsley and Crawford (1984) proposed that because women have been traditionally responsible for shopping and caring for their family, these roles might have increased their exposure to products in supermarkets, pharmacies, and health food stores. On the other hand, Schneider and Nordlund (1983) believed that vanity, and the pursuit of youth and beauty were the primary motives that maintained this practice by women. More recently it has been suggested that the high prevalence of supplement use by women may be an indication of their increased level of awareness about their health and nutritional status (Yu *et al.*, 1999) or that it may reflect a higher level of social acceptance for women, rather than men, to take care of their health (Gray *et al.*, 1986; Wallstrom *et al.*, 1996).

The results of the Georgia Centenarian Study confirm the predictive power of gender on supplement use even among very old women. Female centenarians were five times more likely to report taking supplements compared with men of the same age group (Lyle *et al.*, 1998).

23.4.2 Ethnicity

Several studies have indicated that supplement use is highest among Caucasians, both among the general adult population and in individuals aged 60–65 years and over (Subar and Block, 1990; Bender *et al.*, 1992; Ervin *et al.*, 1999). According to Dwyer (1994) Caucasians may have more economic resources to purchase supplements and better access to advice regarding the benefits of supplement use than other ethnic groups.

23.4.3 Level of education

Data from the US National Health and Nutrition Examination Surveys and the Health Interview Surveys suggest that higher levels of education are positively associated with supplement use in the older American population (Subar and

Block, 1990; Slesinski *et al.*, 1995). Two other studies observed that the relationship between education and supplement use was either gender specific or only applied to particular nutrients. The US Boston Study showed that in older females, higher educational levels were associated with the use of riboflavin, niacin, folate and calcium. However, no such association was observed for older males (Hartz *et al.*, 1988). In another study, well-educated older Australian women more frequently reported the use of vitamin E and vitamin C preparations, compared with women with lower levels of education (Horwath and Worsley, 1989).

23.4.4 Dietary adequacy

There is agreement that supplement users have diets that are overall more nutrient dense than non-supplement users (Hartz *et al.*, 1988; Looker *et al.*, 1988; Kim *et al.*, 1993).

In a study of independently living older Australians (Horwath and Worsley, 1989) found that regular supplement users ate more fruit, vegetables, cereal foods and dairy products more often and also drank more water than non-supplement users or irregular supplement users. Furthermore, older supplement users were more inclined to adopt healthier cooking practices and report that they were following diets that were low in salt, fat or weight reducing. One study of older Americans found that users of the highest level of supplemental vitamin C typically consumed a diet lower in the percent of energy as fat, containing significantly more cruceriferous and red/orange vegetables and obtained higher amounts in nine out of 12 micronutrients, compared with non-users (Lyle *et al.*, 1998).

23.4.5 Cigarette use

Relatively few national surveys have obtained data related to the smoking habits of supplement users, and little is known about the smoking status of specifically older supplement users. In the general adult population, never and former smokers are more likely to use supplements compared with current smokers (Block *et al.*, 1988; Subar and Block, 1990). There is some evidence to show that older supplement users are also more likely to report a lower rate of smoking than non-supplement users (Magarey *et al.*, 1993; Brownie and Myers, 2003).

23.4.6 Health conditions

In an early study of supplement practices of older Australians, Horwath and Worsley (1989) showed that supplement users and non-users did not vary significantly in the number of bouts of illness or visits to their general medical practitioner. However, a more recent investigation of supplement use among independently living older Australians did reveal differences in the health profile

of supplement users compared with non-users. Sufferers of chronic musculoskeletal ailments such as arthritis, osteoporosis and back or neck problems were significantly more likely to report the use of some form of dietary supplement or health preparation (Brownie, 2006). This study, and other investigations (Houston *et al.*, 1998; Yu *et al.*, 1999) also found that on the other hand, some chronic health conditions such as hypertension, diabetes, and heart disease, were barriers to supplement use in the older population.

23.5 Types of supplements consumed by older people

The types of nutritional supplements used most often by independently-living older individuals are preparations containing vitamin C, multivitamins/minerals, vitamin E, fish oils, calcium, garlic and B vitamins (Slesinski *et al.*, 1995; Ervin *et al.*, 1999; Yu *et al.*, 1999; Brownie and Rolfe, 2005). Not surprisingly, there is a relationship between the types of products consumed and the types of health conditions experienced, in this age group. In an early study of older American supplement users, Read and Graney (1982) found that individuals with cardiovascular disease were more likely to report the use of vitamin E while those with arthritis were more likely to report the use of vitamin C and vitamin E preparations.

The US Beaver Dam study found that among participants aged 65–74 years, 33% of women and 27% of men reported the use of a multi-nutrient preparation; 43% of women and 33% of men used vitamin C and 37% of women and 29% of men used vitamin E (Lyle *et al.*, 1998). Supplement use was unrelated to self-perceived health status but was related to gender, age and specific health conditions. Users of vitamin E were 3.2 times more likely to be females, aged approximately 75 years with a previous history of cancer. Men aged 55–64 years with a history of cataracts were more likely than those without such a history to take vitamin E preparations.

Houston *et al.* (1998) examined the supplement practices of independently living older individuals aged 60 years and over. The use of vitamin/mineral preparations were reported by 28% of the sample, followed by vitamin C (13%), calcium (8%) and vitamin E (7%). Approximately 5% or less of the sample reported consuming supplements containing vitamin B12, vitamin D, iron, zinc and magnesium. More than one third (38%) of the participating centenarians had used at least one vitamin or mineral supplement in the previous year (Houston *et al.*, 1998).

The British National Diet and Nutrition Survey of people aged 65 years and over assessed the prevalence of dietary supplements use in predominantly independently living community residents. Using a four-day weighed dietary record (Bates *et al.*, 1998) found that 22% of the sample consumed at least one dietary supplement during this period. Interestingly, the most commonly used dietary supplement was cod liver oil (18%), followed by single vitamins (4%), multi nutrient preparations (4%) and evening primrose (<2%).

23.6 Motivation for supplement use

Users of dietary supplements are motivated by personal beliefs that involve perceptions about the adequacy of their diet, and the role nutrients play in the prevention and treatment of symptoms and health conditions.

In an Australian investigation, which examined the supplement habits of more than 1200 individuals aged 65 years and over, supplement use was associated with the following commonly cited reasons 'for general protection for my body', 'to maintain health and vitality', 'to relieve specific symptoms or conditions' and 'for protection against a specific illness or condition' (Brownie and Myers, 2003). In this sample, supplement use was only weakly associated with perceptions about dietary adequacy, with approximately 10% of supplement users citing 'to make up for a poor diet' as justification for supplement use. Respondents who used vitamin C and garlic believed these preparations were important in the defense against colds and other respiratory complaints, and viewed multivitamin/mineral preparations as beneficial for general health. This study, and others, has shown that in this age group a desire to enhance energy and stamina are commonly cited reasons for using dietary supplements (Hale *et al.*, 1982; Read and Graney, 1982; Sheehan *et al.*, 1989).

Conner *et al.* (2001) used the Theory of Planned Behaviour to examine beliefs about dietary supplement use and to identify factors that might promote supplement use in a subset of participants in the UK Women's Cohort Study. Important elements in this theory, which are thought to influence health behaviour, are reflected in concepts such as subjective norms, perceived behavioural control, behavioural beliefs, health value and perceived susceptibility to illness. The study showed that women who used dietary supplements reported more positive attitudes, perceived more pressure to use supplements, and reported greater perceived control over the use of supplements, than non-supplement users. Supplement users were also significantly more likely to place a higher value on their health than non-supplement users, and to believe that supplements could modify their susceptibility to certain illnesses.

23.7 Circumstances when nutrient supplementation is indicated

There is consensus that good nutritional status can be maintained by consuming a range of foods, and in most cases diet alone is sufficient to meet individual nutritional and health needs. In a Position Statement about food fortification and dietary supplement use, the American Dietetic Association stated that, 'the best nutritional strategy for promoting optimal health and reducing the risk of chronic disease is to wisely choose a wide variety of foods. Additional vitamins and minerals from fortified foods and/or dietary supplements can help some people meet their nutritional needs as specified by science-based nutrition standards such as the Dietary Reference Intakes' (ADA, 2001).

Some countries (e.g., the US, Australia and New Zealand) have established nutrient reference values (NRVs) for two categories of older people – 51–70 years, and 70+ years. It is important to point out that the recommended intake for calcium, vitamin D and vitamin B6, is actually higher in these older age groups, compared with the general adult population.

Recently, the US food pyramid was adapted for people aged 70 years and over. The modified food pyramid reflects the specific nutritional needs of older people and identifies foods with a high ratio of nutrients to energy (nutrient density). Positioned at the top of the pyramid is a flag for the supplements calcium, vitamin D and vitamin B12, in recognition of the value of these nutrients in reducing the morbidity associated with ageing (Russell *et al.*, 1999).

There are numerous factors, associated with ageing, that threaten the capacity of older people to meet these age-adjusted nutrient intakes. For example, immobilisation and isolation, heavy use of medication, periods of lengthy hospitalisation, depression, as well as retirement from paid work, bereavement, and increasingly frailty can contribute to poor nutritional status (Brownie, 2005). In concert, these factors impact on the ability of the older person to meet nutritional needs or to digest, absorb, utilise or excrete nutrients that are ingested.

The following section will discuss how specific nutrients can improve nutritional status, cognitive and functional capacity, and immunity in the older person.

23.7.1 To address inadequate nutrient intakes and malnutrition

Older people are more vulnerable to inadequate nutrition than younger adults and have a higher risk of nutrient deficiencies (Tonore and Bivona, 1992; Young, 1992). The dietary nutrients that are most frequently found to be below the recommended amounts for older individuals include total calories, thiamine, riboflavin, folate, vitamin A, vitamin D and calcium (Griep *et al.*, 1996; de Groot *et al.*, 1999; Haller, 1999; Foote *et al.*, 2000; Bannerman *et al.*, 2001; Drewnowski and Shultz, 2001).

There is a particularly high prevalence of malnutrition in institutionalised individuals; deficiencies in total energy, protein and nutrients have been observed in 35–65% of hospitalised patients and up to 85% of nursing home residents (Apovian, 2001; Vellas *et al.*, 2001). Malnutrition exacerbates existing medical conditions, increases the risk of complications, leads to a decline in functional status, and is associated with longer hospital stays, early institutionalisation and decreased survival time (Davies and Knutson, 1991; Guigoz *et al.*, 1996; Omran and Morley, 2000). According to Sullivan and Lipschitz (1997), severely undernourished elderly patients admitted to hospital 'experience 2 to 20 times higher complications and death rates compared to diagnostically comparable patients who are well nourished'.

23.7.2 To moderate the cognitive and functional decline associated with ageing

Low levels of calcium and vitamin D increase the risk of osteoporosis, fractures and falls (Vieth, 1999; Vieth *et al.*, 2003), while sub-optimal intakes of folate and vitamin B12 increase the risk of heart disease and dementia (Buchman, 1996; Naurath, 2001; van Asselt *et al.*, 2001).

Calcium

Calcium is essential to the maintenance of bone density and in the regulation of cardiac function, muscular contraction, blood clotting and neural transmission. Calcium nutriture is dependent on a number of variables, including dietary intake of protein, fibre (particularly phytate), phosphate and vitamin D status. Dietary sources of calcium include dairy products, calcium-enriched soy beverages, canned fish with bones, figs, molasses, green leafy vegetables and almonds.

A number of age-related factors reduce the absorption of calcium, particularly among older women. Lowered circulating levels of oestrogen and serum vitamin D impair calcium absorption and metabolism resulting in accelerated bone loss (Drewnowski and Warren-Mears, 2001). Atrophic gastritis, and a decline in active intestinal transport of calcium, can also significantly reduce the amount of calcium absorbed (Hoffman, 1993; Blumberg, 1997; Jensen *et al.*, 2001; Russell, 2001).

Because osteoporotic fractures are a major cause of morbidity for older individuals the relationship between calcium intake and the incidence of fractures, has attracted considerable scientific interest. There is a general consensus that either calcium alone or in combination with vitamin D can attenuate bone loss and is particularly effective at reducing the rate of this loss in post-menopausal women (Hoffman, 1993; Heaney, 2001; Feskanich *et al.*, 2003). Clinical trials suggest that in the presence of inadequate vitamin D ($<10\ \mu g$), inactivity and during menopause, calcium levels of 1200–1500 mg/day are required to significantly reduce the rate of bone loss and the incidence of hip fracture in older individuals (Blumberg, 1997; Thurman and Mooradian, 1997; Heaney, 2001).

Vitamin D

Bone and mineral metabolism is profoundly affected by serum concentrations of vitamin D. In addition to its crucial role in bone metabolism, vitamin D is also associated with muscle strength, hypertension, type 1 diabetes, various cancers (Janssen *et al.*, 2002) and more recently, insulin resistance (Chiu *et al.*, 2004). Most tissues have not only vitamin D receptors but also the hydroxylase enzyme that is required to convert cholecalciferol in to the active form (Chiu *et al.*, 2004).

The main source of vitamin D for most people is ultraviolet radiation i.e., exposure to sunlight. Vitamin D can also be obtained from the diet by consuming fatty fish (e.g., salmon, herring and mackerel), eggs, fortified foods (e.g., margarine and some dairy products) and dietary supplements.

Ageing is associated with a decline in the epidermal concentration of 7-dehydrocholesterol, a decline in the concentration of vitamin D receptors in the small intestine, and a decease in renal conversion of vitamin D into calcitriol, the biologically active form or ($1,25(OH)_2D$).

The objective way to establish vitamin D status is by measuring serum concentrations of the predominant circulating form of vitamin D – cholecalciferol (25OHD) (Vieth, 1999). Although there is no consensus on what represents an optimal cholecalciferol concentration, low serum concentrations, defined in some studies as 25OHD concentrations between 25 and 50 nmol/L, are commonly found in older people and are associated with hip fractures, muscle weakness, reduced functional capacity and elevated serum parathyroid hormone concentrations resulting in increased bone turnover and risk of osteoporosis (Hoffman, 1993; van der Wielen *et al.*, 1995; Lovat, 1996; Need *et al.*, 2000). Data from the SENECA study found that the prevalence of low 25OHD concentrations (defined as serum 25OHD <30nmol/L) in older people in Europe was high (van der Wielen *et al.*, 1995), particularly in southern European countries such as Italy, Greece and Spain, where the risk of osteoporotic fractures is expected to exceed the predictions for the general elderly population of Europeans.

Muscle function, and the risk of falls, is affected by inadequate vitamin D in older individuals. Calcium metabolism by muscle cells is reduced in the presence of insufficient vitamin D, contributing to symptoms of muscle weakness, predominantly of proximal muscles. One study of elderly subjects aged 65 years and over found that 25OHD concentrations in the range of 30–40 nmol/L was associated with reduced handgrip strength, reduced leg extension power, feelings of heaviness in the legs, fatigue, difficulty ascending stairs and rising from a chair (Janssen *et al.*, 2002).

Serum concentrations of cholecalciferol vary among individuals and depend on exposure to ultraviolet radiation and the contribution from vitamin D foods and vitamin D fortified products. According to Vieth (1999) sunlight exposure of the hands and face for 20–30 minutes correlates with the production of approximately 5–10 μg of vitamin D, an amount sufficient to maintain only a modest 25OHD level, i.e. 20–25 nmol/L. The use of sunscreen however inhibits the photoproduction of vitamin D in the skin (Hoffman, 1993). Dietary sources of vitamin D are unlikely to prevent low 25OHD concentrations occurring in this age group. Several studies have shown that older people report diets that provide as little as 2.5–3.5 μg of vitamin D (Blumberg, 1997; Kinyamu *et al.*, 1998).

Older populations at risk of poor vitamin D status, include those who are housebound, institutionalised, and sedentary. Individuals with limited sun exposure and inadequate dietary sources of vitamin D would benefit from a vitamin D supplement of at least 10 μg. Much larger doses of vitamin D are necessary to treat moderate to severe vitamin D deficiency.

When the 1989 edition of the US NRVs were reviewed it was agreed that higher intakes of calcium and vitamin D were needed to reduce the risk of osteoporosis (ADA, 2000). Consequently, the 1999 edition of the US NRVs recommended increased intakes of these nutrients for Americans aged 51–70

years of age, and 70 years and above. For example, the requirement for calcium for individuals aged 51 years and over increased by up to 50% (from 800 to 1000–1200 mg) and vitamin D by up to 150% (from 5 μg to 10–15 μg). The current US, Australian and New Zealand recommendations for vitamin D are 5 μg (0–50 years), 10 μg (51–70 years) and 15 μg (71 years and over). This represents a three-fold increase in the vitamin D requirements for people aged 70 years and over.

Vitamin B12, vitamin B6 and folate

Folate and vitamins B12, B6 participate in numerous metabolic pathways, including the metabolism of amino acids, red blood cells, the synthesis of neurotransmitters, myelin and phosphatidylcholine, as well as other compounds important to the nervous system (Stabler, 2003). These vitamins are also necessary for the regulation of homocysteine: a sulphur-containing amino acid derived from the product of methionine and cysteine metabolism (de Jong *et al.*, 2001; Koehler *et al.*, 2001; Prins *et al.*, 2002). The metabolic pathway for homocysteine removal by remethylation requires folate and vitamin B12, and removal by catabolism requires vitamin B6 (Koehler *et al.*, 2001). It follows then, that insufficient folate, and to a lesser extent vitamin B12 and vitamin B6, can contribute to an accumulation of serum homocysteine.

These nutrients can be obtained by consuming beef, liver, fish and milk (vitamin B12); liver, meats, vegetables, cereal and nuts (vitamin B6), and fortified cereals, liver, legumes, and dark green leafy vegetables (folate).

Impairments in gastric function (e.g., atrophic gastritis) significantly reduce the bioavailability of folate and vitamin B12 and contribute to the rise in homocysteine levels observed in the older person (Carmel, 1997). Other factors that contribute to elevated homocysteine levels include alcohol and coffee consumption, smoking, abnormal renal function and inborn errors of homocysteine metabolism (Lovat, 1996; Salvioli, 1998; Brattstrom and Wilcken, 2000; Mennen *et al.*, 2002).

At elevated levels homocysteine is considered an independent risk factor for heart disease, stroke, peripheral vascular disease, venous thrombosis (Salvioli, 1998; Carlson, 2000; Evans *et al.*, 2000; Finn, 2000; Prins *et al.*, 2002; Obeid *et al.*, 2004) and is the most frequent biochemical marker of patients with neurological disorders, such as dementia and Alzheimer's disease (Finn, 2000).

When the 1989 edition of the US NRVs were reviewed it was agreed that the levels for folate and vitamin B12 were insufficient to suppress homocysteine levels to within normal range (ADA, 2000). Consequently, the 1999 edition of the US NRVs recommended increased intakes of these nutrients for Americans aged 51–70 years of age, and 70 years and above. For example, the requirement for folate for individuals aged 51 years and over increased by more than 100% (from 180–200 μg to 400 μg) and vitamin B12 by 20% (from 2.0 μg to 2.4 μg).

23.7.3 To enhance immune function

Ageing is associated with a decline in immune function, in particular cell-mediated response, thereby predisposing the elderly to increased rates of infection. The impaired immune response present in the older person may be the consequence of normal ageing or result from chronic pathological conditions or poor nutritional health. Immunological studies have shown that protein-energy malnutrition can significantly reduce cell-mediated immunity, phagocyte function, complement system, secretory immunoglobulin A antibody concentrations and cytokine production (Cason *et al.*, 1986; Chandra, 1997). In respect to the micronutrients, zinc, selenium, iron, copper, vitamin A, vitamin C, vitamin E, vitamin B6 and folic acid, are important determinants of immune function (Chandra, 1997; Lesourd and Mazari, 1999), and as previously discussed, are often lacking in the diets of older people.

Several studies have investigated the effect of multi nutrient and single nutrient supplementation (e.g., vitamin C, vitamin E, zinc, selenium, etc.) on immune function in this age group, with varied study sizes, methodologies and results (Kennes *et al.*, 1983; Cossack, 1989; Chandra, 1992; Bogden *et al.*, 1994; Meydani *et al.*, 1997; Pallast *et al.*, 1999; McKay *et al.*, 2000). A critical evaluation of the current literature is beyond the scope of this chapter, and readers are directed to a recent literature review for more information on this topic (Mitchell *et al.*, 2003). This section will be restricted to examining the effects of multi-nutrient supplementation on immune function, in this age group.

The main outcome measures of immune function reported in the literature are the incidence of infections, lymphocyte production (e.g., antibodies and T-cells), and the results of delayed-type hypersensitivity skin tests. In an RCT, low dose supplementation of multiple vitamin and minerals for 12 months, in a small sample (n=96) of individuals aged 66–86 years, was associated with a significant improvement in lymphocyte counts, natural killer T cell activity, and self-reported illness. Furthermore, supplement users reported significantly fewer days of infection per year and fewer days of antibiotic use compared with control (Chandra, 1992). Other RCTs have found similar improvements in lymphocyte proliferation and activity, and increases in delayed type hypersensitivity tests related to multi-nutrient supplement use (Bogden *et al.*, 1994; Pike and Chandra, 1995; Buzina-Suboticanec *et al.*, 1998). In general, the literature confirms that multi-nutrient consumption has a positive impact on immune function, particularly among elderly individuals with poor nutritional status.

23.8 Potential problems associated with supplement use

Evaluating the risks associated with supplement use in the older age group is confounded by the lack of experimental evidence on the topic of drug interactions; discrepancies in the literature regarding the dosages at which adverse effects or interactions are most likely to occur; the paucity of studies

that have assessed the extent of concurrent use of prescription and over-the-counter medication, including dietary supplements; and, uncertainty about the toxicity of high dose nutrient intakes in the older person. Although Tolerable Upper Levels have been established for several nutrients, these values do not represent the level at which toxicity reactions might occur.

23.8.1 Interactions between nutrients and/or drugs

Nutrients interact with each other and with other components in the diet. Therefore, long-term exposure to high levels of particular nutrients may have a detrimental effect on the absorption of other nutrients or drugs. For example, large doses of vitamin C can inhibit the action of Warfarin; vitamin E can potentiate the action of antiplatelet/anticoagulant medication and calcium and zinc interfere with the absorption of tetracycline and fluoroquinolone antibiotics. The action of calcium channel blockers, a class of drugs that lower high blood pressure, may be reduced in concurrent users of high dose calcium supplementation (Skidmore-Roth, 2001; Bratman and Girman, 2003; Braun and Cohen, 2005).

The literature confirms that a significant portion of older supplement users is at risk of an interaction occurring. Studies have shown that between 33% and 50% of dietary and herbal supplement users aged 65 years and over take at least one combination of a health product and prescription or over-the-counter drug that could cause an interaction (Dergal *et al.*, 2002; Ly *et al.*, 2002).

23.8.2 Lack of disclosure about supplement use to health professionals

The rate of disclosure about supplement use to physicians, and other health professionals, is not well understood. Few studies have specifically examined this aspect of supplement behaviour. Based on the available data it appears that underreporting this use is common among the general adult population. Giveon *et al.* (2004) found that 45% of general practice patients who used supplements did not disclose this information to their physician, despite the fact that almost half (49%) were also taking prescription medication. The majority of supplement users (56%) were of the opinion that supplements were safe and free of side effects – a perception that most probably contributed to the high rate of non-disclosure in this sample. Another study confirmed that users of herbal medicine also appear to withhold this information: 60% of general practitioner patients who used these preparations failed to report this to their physician (Klepser *et al.*, 2000).

One small study of elderly American veterans found that more than one-third (35%) of dietary supplement users had not disclosed this information to their health care provider (Ly *et al.*, 2002). This finding is consistent with an Australian study, which found that approximately one-third (32%) of supplement users aged 65 years and over rarely if at all, reported the use of supplements to their doctor (Brownie and Myers, 2003). According to Eisenberg

(1997), distrust and lack of rapport are frequently cited reasons for supplement use not being disclosed to practitioners. This lack of communication might also suggest that physicians need to incorporate a thorough assessment of all supplements consumed as part of the history taking and medication review. Failure to disclose information about supplement use could place older individuals at increased risk of a drug-supplement interaction.

23.9 Sources of further information and advice

For more information about contraindications and precautions associated with vitamin, mineral and herbal preparations and interactions with pharmaceutical drugs, readers should consult the following books: *Handbook of Herbs and Supplements and their Therapeutic Uses* (Bratman and Girman, 2003), *Clinical Guide to Nutrition and Dietary Supplements in Disease Management* (Jamison, 2003), *An Evidence-Based Approach to Vitamin and Minerals* (Higdon, 2003), and *Herbs and Natural Supplements* (Braun and Cohen, 2005).

23.10 Conclusions

In summary, nutrient supplement use in the older age group tends to be a marker for a number of positive dietary and health-related behaviours. Older supplement users are typically female, Caucasian, well educated, with healthier dietary habits and are less likely to smoke compared with non-supplement users. They commonly report the use of preparations containing vitamin C, multivitamins/minerals, fish oils and vitamin E. The popularity of this practice is evidence that older people take an active role in preventative health care, and believe that supplements can minimise their suffering, arrest deterioration and prolong functional independence. The literature suggests that supplements can assist older people attain their age-adjusted recommended nutrient intakes and subsequently reduce the burden of chronic disease in this age group. Indiscriminate use of supplements, and failure to report the use of these products to health care providers probably represents the greatest risk associated with this behaviour.

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Part III

Developing food products and services for older people

24

Food safety and older people

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Tell us of more than one incident where somebody got sick and died.
Focus Group Participant

Abstract: As one ages, there is a greater risk of developing a foodborne illness and the complications can be more serious. Many food handling practices, perceived consequences of mishandling food, barriers to making changes, sources of knowledge, and desired educational methods of this population are different from those of the general population. This chapter expands upon these differences and provides suggestions on how to meet the educational needs of senior citizens. It also provides an explanation of why the ageing population is at greater risk and the pathogens of greater concern. Because foodborne illness in this population will continue to be a top concern throughout the world, a discussion of specific practices that will make an impact to reduce the risk is included as well as suggestions to motivate this group to attend educational programs.

Key words: food safety, foodborne illness, food handling, food handling behaviors, home delivered meals, seniors.

24.1 Introduction

Eating, an enjoyable activity for most people, has become more complicated as the awareness of the safety issues of our food supply around the world grows. This will likely continue as media exposure of these issues intensifies. With the globalization of the food supply, along with the introduction of pathogens into this supply, picking up a food and eating it without a thought can be a hazard to one's health.

The normal physical changes as one ages, along with improper hygiene and food handling practices, places an older person at greater risk of developing a

foodborne illness. As compared to the general public, the complications of a foodborne illness in the ageing population can result in more serious complications.

Along with specific food handling behaviors, pathogens of concern to the ageing population have been identified. The ageing population's current food handling behaviors, perceived consequences of mishandling food, barriers to making changes, sources of knowledge, and desired educational delivery methods may be quite different than those of the general population. For example, some elderly report that a source of their cooking knowledge was their grandmother (Gettings and Kiernan, 2001). In reality, that means they learned food handling practices from more than 100 years ago!

By the year 2030, it is estimated that greater than one billion individuals worldwide will be 65 years of age and older (US Census Bureau, 2005). As this population ages, so does the need for more nursing home care and home-delivered meals. Addressing the food safety educational needs of the older population, as well as educating those providing food service to this group, is of utmost importance.

The elderly are vocal on how and where they prefer to receive their educational messages. They provide a wide range of opportunities for health care professionals and educators to provide these messages. Owing to their increasing numbers as a percentage of the population and because they are at increased risk for foodborne illness, health professionals and scientists have a responsibility to conduct research in this area and to educate this subgroup of the population.

24.1.1 Incidence and complications of foodborne illness

In the general population, it is estimated that each year 76 million Americans, 2.1 million to 3.5 million British (Mead *et al.*, 1999), 4.7 million Australians (Australia New Zealand Food Authority, 1999), and 130 million Europeans (World Health Organization (WHO), 2000) experience a foodborne illness. Annual rates of foodborne illness are estimated to be approximately one per four cases in the United States (Mead *et al.*, 1999) and one per five cases in England (Wheeler *et al.*, 1999). Those from England, Wales, the United States, and Australia may suffer from foodborne illness at least once every 4.5 to 5 years (Redmond, 2002).

While younger individuals usually face higher rates of infection from foodborne pathogens (bacteria, fungi, parasites, viruses, and their toxins), older adults are likely to have more serious complications from these infections. In fact, research has shown that the elderly are more susceptible to gastroenteritis-induced deaths (Buzby, 2002; Lew *et al.*, 1991). Examination of data from the US Hospital Discharge Survey between 1979 and 1995 reveals that hospitalization rates for adults with gastroenteritis was highest (7.6 hospitalizations per 1000 persons) among adults 75 years of age and greater. Mean length of stay and case-fatality rates for adults hospitalized with gastroenteritis also increased with age. In addition, those in the 75 and above age group were 33 times more likely

to die during hospitalization for gastroenteritis as compared to those 20–49 years of age (Mounts *et al.*, 1999).

The United States Food and Drug Administration (FDA) estimates that two to three percent of all acute foodborne illnesses develop secondary long-term complications called chronic sequellae. These sequellae can occur in any part of the body, such as joints, nervous system, kidneys, and/or heart. One chronic sequellae from *Campylobacter* infections that particularly afflicts older adults is Guillain-Barre Syndrome, which is an autoimmune disease that can cause paralysis (Buzby, 2002).

24.1.2 The ageing population at risk

It is well documented that the ageing population is considered a high-risk population for foodborne illness. What has not been documented is at exactly what age does one's risk increase. In addition, there has been consideration that there is a group of healthy elderly and a group of unhealthy elderly. Can we place all these people in one group and say they are all at increased risk? Or, should we take a look at the possibility that the unhealthy elderly as a subunit of this group are at a greater risk of foodborne illness?

As a population, older adults vary widely in terms of physiological function, health, and susceptibility to disease (Buzby, 2002; American Dietetic Association (ADA), 2000; Smith, 1998). Many of the ageing population in the age range of 65–84 enjoy sufficient health for full physical function. But for those 85 years of age and beyond, we see an increased risk for both infections and death from infections, including foodborne illness. This is due to a decrease in immune function associated with ageing, chronic diseases, and health issues like malnutrition and immobility (Strasbaugh, 2001; Smith, 1998; Gerba *et al.*, 1996).

Several factors result in the ageing of the immune system. Intestinal motility and mucosal immune function decrease with normal ageing, increasing the susceptibility to systemic infection via the gut (Bitar and Patil, 2004; Fujihashi and McGhee, 2004). In addition, the overuse of H2-receptor antagonist and over-the-counter antacids to treat gastroesophageal reflux disease, which is common among older adults, is a concern. This may cause hypochlorohydria and further reduce the ability to resist infection by allowing more ingested pathogens to enter the intestinal tract (Donskey, 2004; Mead *et al.*, 1999; Smith, 1998). Along with these medications, the prolonged use of antibiotics can stimulate overgrowth of colonic pathogens and result in the loss of competitive inhibition provided by the gut's natural microflora (Donskey, 2004).

Reduced intestinal motility also places the older person at higher risk of a foodborne illness. The decreased contractions that push food through the intestine slows the time it takes to eliminate pathogens from the intestinal tract and allows more time for toxin formation and damage (Buzby, 2002; Smith, 1998). A defective constitutive functioning of macrophages and granulocytes

and the natural shift to memory T-cells with ageing reduces the elderly's ability to mount a cell-mediated response when exposure to new pathogens occurs (Castle, 2000; Khanna and Markham, 1999).

Therefore, the susceptibility to foodborne illness can increase for the elderly when they are exposed to newly emerging or genetically-mutated pathogens (Kendall, 2006). In addition, dehydration as a result of decreased consumption of fluids can also reduce the effectiveness of the immune system (Buzby, 2002; Smith, 1998). The sensation of feeling thirsty commonly declines with age; therefore placing older adults at risk of dehydration if they rely on thirst to determine their need for fluid.

Various chronic diseases and the regimens to treat these diseases place the elderly at increased risk for infection (Bitar and Patil, 2004). For those 65 years of age and older, the leading causes of death are often related to a compromise in the immune system (Center for Disease Control (CDC), 2002). For example, 70% of deaths due to cancer occur among the elderly (Ershler, 2003). Diabetes mellitus, which affects 18–25% of persons 65 years of age and older, can promote systemic pathogenic infection through persistent hyperglycemia (Maldonado *et al.*, 2004; Umpierrez and Kitabchi, 2003) and loss of microcirculation efficiency (Dinh and Veves, 2005).

A variety of factors place the elderly at greater risk of malnutrition (see Chapter 14 by Lesourd and Ferry). As a result of numerous nutrient deficiencies, the risk of infection increases (see Chapter 8 by van Staveren and Morley). Malnutrition can also affect one's taste acuity and result in eating food that has significant bacterial growth (Winkler *et al.*, 1999; Prasad *et al.*, 1993).

While the research on the effects of cognitive impairment on risk of infection is not clear, a study of patients with Alzheimer's disease found further impairment of cognitive function after infection due to increased levels of IL-1 beta (Holmes *et al.*, 2003).

A loss of mobility can also negatively affect immune function. Sedentary elderly clients have lower levels of IL-2, IL-4, and IFN y3 as compared to elderly male runners (Shinkai *et al.*, 1995). A review study by Kohut and Senchina (2004) concluded that long-term exercise intervention may be useful in improving immune function in the elderly.

24.1.3 Source of foodborne illness – location

Studies have revealed that the general consumer views food manufacturing and production as the most likely place for contamination to take place (Williamson *et al.*, 1992). A survey of 3120 consumers, conducted by the United Kingdom's Food Standards Agency (FSA) in 2002, who claimed to have suffered food poisoning in the past 12 months, revealed that only 21% believed the cause of the illness was food prepared at home. Epidemiological data from the WHO surveillance of Foodborne Infections and Intoxications supports this belief. Data from the WHO from 1993–1998 reveals the percentage of foodborne outbreaks associated with preparing foods in one's home as follows:

- England and Wales 12%
- Germany 39%
- Spain 49%
- France 58%

There are several issues that make determination of the source of contamination difficult. According to the FSA (2000) and Lerman (2001), the majority (over 95%) of cases of foodborne illness are believed to be sporadic. These cases, as well as small outbreaks that originate in the home, typically involve individuals or a small number of people, and are less likely to be reported to public health officials (Worsfeld and Griffith, 1997; Knabel, 1995). Therefore, the actual cases of foodborne illness originating from the home are likely to be much larger that has been reported (Zhao *et al.*, 1998).

Locations that have been most frequently implicated as a source of foodborne outbreaks are restaurants, cafeterias, and bars. However, Borneff and colleagues (1988) reported that foodborne illness from foods consumed in private homes is three times more frequent than that from foods consumed in cafeterias. In fact, up to 87% of reported foodborne outbreaks in United States, United Kingdom, Europe, Australia, New Zealand, and Canada have been associated with food prepared or consumed at home (Tirado and Schmidt, 2000).

24.1.4 Pathogens of concern

The Foodborne Disease Active Surveillance Network (FoodNet) of the Center for CDC in the United States uses active surveillance and epidemiological studies to provide national estimates of the burden, trends, and sources of specific foodborne disease in the United States. As reflected in this data, pathogens of particular concern to the elderly are *Campylobacter*, *E. coli O157:H7*, *Listeria*, *Salmonella*, *Vibrio*, and Norovirus.

FoodNet data from 2003 show that compared to younger adults (ages 20–59), persons 60 years of age and older have a higher incidence of infection caused by *E. coli O157:H7*, *Listeria*, *Salmonella*, and *Vibrio* (CDC, 2003). While FoodNet data does not report information on *Clostridium perfingens* and *Staphylococcus aureus*, it has been reported that the elderly are at increased susceptibility to these bacteria, also (Smith, 1998). From 1996–2001, FoodNet data shows that hospitalization rates for persons 60 years and older were highest for infections caused by *Listeria species* (96%), *E. coli O157:H7* (67%), *Vibrio species* (49%), *Salmonella species* (49%), and *Campylobacter species* (28%) (Ailes *et al.*, 2004).

The number of campylobacter infections in the ageing population is actually lower than for young adults; however, the rate of hospitalization of those 60 years of age and above and diagnosed with *Campylobacter* species is more than twice the rate of any other age group (Samuel *et al.*, 2004; Ailes *et al.*, 2004). As mentioned before, Guillain-Barre syndrome can be triggered by *Campylobacter jejuni* and is a significant cause of mortality among those in the 70–79 age bracket (Prevots and Sutter, 1997).

Rangel and colleagues (2005) reported *E coli O157:H7* has been involved in 52% of the foodborne outbreaks between 1982 and 2000. For those in residential facilities, i.e. hospitals and nursing homes, a case-fatality rate of 6.6% is 13 times higher than the overall case-fatality rate of 0.5%.

Listeria monocytogenes is found most frequently in ready-to-eat foods and is widely present in the environment. Those who are more susceptible to *Listeria* include those with underlying conditions that interfere with T-cell mediated immunity (Rocourt, 1996). In reports of two *Listeria* outbreaks, the elderly had the highest rates of infection and mortality (Goulet and Marchetti, 1996; Bula *et al.*, 1995). Liver disease and use of gastric acid-reducing medication also place people at additional risk for *Listeriosis* (Varma *et al.*, 2004).

Among persons infected with *Salmonella*, those age 60 and older have the highest rates of hospitalization and death (Kennedy *et al.*, 2004; Trevejo *et al.*, 2003; Voetsch *et al.*, 2004a). Vibrio infections in the United States are highest in this same age group, and those with infections from *Vibrio vulnificus* are more likely to result in illness, hospitalization, and death as compared to other Vibrio species (Voetsch *et al.*, 2004b). Those afflicted with liver disease, alcohol use, and compromised immune system are at an even greater risk of being infected with *Vibrio*.

The Norovirus is a highly infectious agent and may account for as many as 50% of the outbreaks in the United States (Widdowson *et al.*, 2005). In addition, the majority of outbreaks of gastroenteritis in institutions, like nursing homes and hospitals, are caused by norovirus (Koopmans and Duizer, 2004).

Based on data of the pathogens of most concern to the ageing population, information regarding research on the food-handling practices, perceived consequences of mishandling food, barriers to make changes, sources of knowledge, and desired educational delivery methods will be highlighted

24.2 Food handling behaviors and practices

24.2.1 Food storage

Several focus group studies looking at a variety of food safety behaviors and practices among the ageing population have been conducted. A study conducted by Johnson and colleagues (1998) and a follow-up study by Hudson and others (2002) in the United Kingdom concluded that a large portion of elderly people keep their refrigerator at a temperature too warm to inhibit the growth of harmful microorganisms. They also found the majority of the women had not measured their refrigerator temperature and did not know what it should measure. Comments such as ‘The man set it up for me when it was delivered’ and ‘My husband used to do all that, and I haven’t touched it since he died’ were made. The general opinion of respondents was they would know if their refrigerators were working by the feel of the food inside.

Given the additional finding that print size was too small and cramped and poor eyesight uncorrected by glasses are the two main reasons for poor label

readability, it is therefore reasonable to conclude that larger, clearer labels with proper food storage recommendations could contribute to improved food safety storage in this age group. The follow-up study also looked at 'use-by' and 'best before' dates. Two-thirds of the participants considered it of greatest importance when reading food packaging information. While the participants seemed to understand the importance of these dates, the dates were not necessarily adhered to. Several participants bought items near to the end of the product shelf-life as they were cheaper. Although they appreciated that these dates related to safe food, they kept items for up to a month prior to consuming them.

24.2.2 Food preparation

Hudson and others also looked at the methods of defrosting foods and found half the participants defrosted perishable food items on the kitchen counter while the other half did so in the refrigerator. Due to the fact that the majority of refrigerator temperatures were above the recommended temperature, the proper practice of placing foods in the refrigerator within the proper amount of time will still increase one's risk of foodborne illness. While the majority of cutting boards present in all of these kitchens were plastic and most respondents stated they washed cutting boards in between tasks, dishcloths were replaced anywhere from one to two times per week to one time per month. Most of the washcloths were left 'wrung' wet on draining boards. The misuse of dishcloths increases the risk of cross-contamination, of which consumers may not be aware.

A seminal study by Gettings and Kiernan (2001) used focus groups to look at several food safety practices, the consequences of not handling food safely, barriers to change, and what is needed to change inappropriate practices in Pennsylvania elderly. Seventy-four people 60 years of age and older from a mix of rural and urban areas who prepared meals at home participated in the study (see Table 24.1).

In the area of cooking, the inappropriate practices that were found to be extensive included relying on a specific amount of time, using utensils to cut food open, and using sight alone; e.g., 'if you take chicken out and you see blood, then you know you have to leave it in longer.' Other inappropriate practices considered to be substantial were using touch and utensils to feel the consistency and tension of food; e.g., 'I wiggle the turkey leg. If it's loose, I guess it's done.' The reliance on pop-up thermometers to determine if a food had been adequately cooked was found to be limited. When it comes to the consequences of not using a thermometer, the participants' awareness was negligible. While the use of the appropriate practice of using a meat thermometer to determine whether a food is cooked to the correct temperature was found to be extensive, it must be noted that it was mainly used only on large pieces of meat and poultry.

When it came to cooling food, there was extensive evidence that the elderly place large quantities of hot food, without portioning it into smaller quantities, directly into the refrigerator. Awareness of the consequences of not properly cooking foods was limited. On the other hand, there is extensive evidence that

Table 24.1 Repetition across focus groups and its classification

When a category in the study existed across:	Repetition in the data was classified as:
Five or six focus groups	Extensive
Three of four focus groups	Substantial
Two focus groups	Limited
One focus group	Negligible

From Gettings and Kiernan (2001).

this group used two appropriate cooling practices. These included placing food that has been on the counter for less than two hours in the refrigerator and cutting and separating large portions that are hot into smaller portions and placing them in the refrigerator within two hours.

In the area of thawing foods, the ageing population's extensive inappropriate practice was that of placing frozen food in water that is never changed; e.g., 'Turkey makes the water cold so you don't have to change it ... done this for years and it hasn't hurt us yet.' The research revealed there is limited evidence that the elderly place frozen food on the counter for more than two hours and place it in the microwave and then refrigerate it, two additional inappropriate practices. The awareness of the consequences of not thawing foods correctly was extensive and fell into two categories: affecting their health (becoming ill and/or dying) and their food (an increase in bacteria and spoilage). The researchers found extensive evidence that the elderly have used four practices to properly thaw frozen food:

1. place in the microwave
2. place in water not running but changed
3. place in a refrigerator
4. place directly in an oven.

Another focus group study by Boone and colleagues (2005) revealed similar findings. Mature adults generally had knowledge of safe food handling but did not refrigerate foods promptly and did not use a meat thermometer. The groups also expressed a concern about lack of knowledge about cleanliness and food safety knowledge. In addition, they were also worried about lack of control over food preparation outside the home; e.g., 'They are preparing this food without gloves and that kind of thing. I am concerned about that.'

In a study by Altekruse and colleagues (1999), those over the age of 60 (as compared to those under that age) were much more likely to report consumption of undercooked eggs than any other risky behavior. Because eggs are relatively inexpensive, easy to prepare, and are well liked, the risk of *Salmonella enteriditis* is an area of concern (Kendall *et al.*, 2006).

24.2.3 Barriers to changing behavior

When the seniors were told the safest ways to cook, cool, and thaw foods in the Gettings and Kiernan focus group study and then asked if they would be willing to always change these practices, the seniors who used inappropriate practices revealed barriers in two of the three areas. Their resistance to thaw foods properly and use a thermometer to assure their foods were cooked adequately was extensive. They justify their old ways; e.g. 'Our food is so overcooked, it would go above the recommended temperatures.' They also perceived some changes as an adjustment and inconvenience; e.g., 'I can't be bothered to use a thermometer.' Another barrier, lack of resources, was also extensive. This group did not own, couldn't afford, or didn't know how to use a thermometer. Other barriers for thawing properly include things happening at the last minute, a full refrigerator, and the cost of throwing out food. Barriers found by Boone and colleagues included time, prior knowledge, food appearance, tradition, skepticism, and habit.

When asked what they needed to know to be convinced to always thaw foods properly and to use a thermometer to make sure foods are cooked to the correct temperature, the participants want to know the health effects, e.g., 'Tell us more than one incident where somebody got sick and died,' from credible sources, particularly educators.

24.2.4 Sources of knowledge

Gettings and Kiernan (2001), Boone and associates (2005), and Hudson and Hartwell (2002) found when the elderly are asked how they learned about practices they currently use to cook, cool, and thaw foods, several sources were identified and include:

- learning on the job and over time
- relatives (grandmothers and mothers, children, grandchildren, and wife)
- written methods (magazines, newspapers, and package directions but not brochures)
- verbal methods (radio and television)
- educational programs
- internet
- cooperative extension flyers and inserts
- health food stores.

24.3 Changing behavior

24.3.1 Food safety messages for the ageing population

To be most effective, food safety education should target changing those behaviors that will most likely result in illness (Medieros *et al.*, 2001a). But, the elderly believe that most of the food handling behaviors they practice are not making them ill (Gettings and Kiernan, 2001). In addition, when consumers

underestimate the frequency or seriousness of foodborne illness, they are less interested in making behavior changes (Fein *et al.*, 1995).

Based on the factors, or constructs, that influence perceptions of risk, Sandman (1987) argued that microbes in food represent a high hazard that elicits low outrage. According to psychometric approaches to understanding risk perception, home-based food safety issues have characteristics that result in lay people psychologically underestimating the threats. In addition, there is a belief that foodborne illness most likely originates from food-handling procedures at food-processing plants and restaurants (Williamson *et al.*, 1992) rather then in their own home (Food Standards Agency, 2002) where they believe they have control. These are all issues that need to be addressed and taken into consideration when developing food safety education for the ageing population.

Based upon the food sources of the specific pathogens associated with and the food safety errors practiced by the ageing population, Medeiros and her associates (2001b) suggest that food safety curricula and materials should emphasize five major pathogen-control factors. These control factors include:

- practice personal hygiene
- cook foods adequately
- avoid cross-contamination
- keep foods at safe temperatures
- avoid food from unsafe sources (including ready-to-eat foods produced or processed in a manner that does not ensure pathogen reduction).

These areas also address the inappropriate food handling practices in the various studies and include improper refrigeration temperatures and improper handling of dishcloths, along with improper cooking, cooling, and thawing.

Kendall and associates (2003) used a four-round, Web-based Delphi process with nationally recognized food safety experts to identify 14 food-handling and consumption behaviors (see Table 24.2) of special importance for elderly persons. Nine of these behaviors are best controlled by avoiding foods from unsafe sources, a control factor that has not been traditionally addressed in food safety curricula and programs. Many of the behaviors are associated with avoiding raw or undercooked foods (seafood, eggs, and sprouts) and foods association with *Listeria monocytogenes* (soft cheeses, cold smoked fish, cold deli salads luncheon meats, and cold hot dogs).

24.3.2 Delivery methods for the ageing population

According to Bodkin and LaSlavia (1996), it is imperative that risk-reduction health campaigns (such as ones focusing on food handling strategies) address the specific and needs of the target population.

Research found that the ageing population uses a wider array of inappropriate food safety practices as compared to the general public, clearly establishing a need to target this audience with food safety messages specifically designed for them (Boone *et al.*, 2005; Gettings and Kiernan, 2001). The 2001 study also

Table 24.2 Consumer food handling behaviors of special importance to elderly and immune compromised individuals

Behavior[a]	Pathogen
Avoid eating raw and undercooked seafood	*Vibrio* species
Avoiding eating raw sprouts	*Escherichia coli* O157:H7
Avoid soft cheeses, cold smoked fish, and cold deli salads	*Listeria monocytogenes*
Avoid eating foods containing raw eggs	*Salmonella* Enteritidis
Avoid hot dogs and lunchmeats that have not been reheated to steaming hot or 165 degrees Fahrenheit	*Listeria monocytogenes*
Use cheese and yogurt made from pasteurized milk	*Salmonella* species
Cook shellfish until the shell opens and the flesh is fully cooked; cook fish until flesh is opaque and flakes easily with a fork	Norwalk-like viruses
Obtain shellfish from approved sources	Norwalk-like viruses; *Vibrio* species;
Drink only pasteurized milk and fruit juices	*Escherichia coli* O157:H7; *Listeria monocytogenes*; *Salmonella* Enteritidis; *Campylobacter jejuni; Yersinia enterocolitica*
Store eggs and poultry in the refrigerator	*Salmonella* Enteritidis
Wash knives, cutting boards, and food preparation surfaces with hot water and soap after contact with raw poultry, meat, and seafood	*Salmonella* species; *Campylobacter jejuni; Yersinia enterocolitic; Listeria monocytogenes*; *Toxoplasma gondii*; *Salmonella* Enteritidis; *Escherichia coli* O157:H7 *Vibrio* species; *Shigella* species
Thoroughly rinse fresh fruits and vegetables under running water before eating	*Escherichia coli* O157:H7
Cook eggs until both the yolk and white are firm. Use a thermometer to make sure that foods containing eggs are cooked to 160 degrees Fahrenheit	*Salmonella* Enteritidis

[a] Behaviors that are greater than or equal to 80% of a national panel of food safety experts ($n = 28$) rated as being of special importance to the elderly and/or immunocompromised individuals, with those rated as important to both groups presented first.
From Kendall *et al.* (2003).

found that this group will use appropriate practices if they are told that inappropriate practices are linked to a real threat to their health from illness and/or death; i.e., 'Tell me my life depends on it.' The research also supports and clarifies other findings about how to deliver education regarding foodborne illness. First, despite the elderly's reliance on the past, i.e. on relatives (mostly grandmothers and mothers) and their own experience of having used

inappropriate practices without becoming sick, the elderly want information on proper food safety practices. When the researchers asked the elderly about preferred methods for food safety education, they discussed two aspects – the methods themselves and the location. Support was extensive for written educational pieces (brochures, flyers, and pamphlets), television, and video; e.g. 'Have videos available at the senior center and library to take home so we can look at them whenever we want.' There was substantial support for newspapers, radio, and church bulletins, but only limited support for computers at senior centers, recipe cards, and magazines. When this group discussed location, support for education is extensive in churches and physician/dentist offices and substantial for health centers. Boone and associates' (2005) focus group research revealed similar and additional areas to disseminate information – doctor's offices, the grocery store meat counter, and through workshops at senior centers.

24.3.3 The use of videos and educational pieces

Two different videos were viewed by the participants of two of the focus group studies. The support for humor was extensive, as was the desire for people other than the elderly, especially if the video is depicting an inappropriate behavior (Gettings and Kiernan, 2001). The focus group participants also prefer videos that are not condescending (address them as though they were children) (Boone *et al.*, 2005).

When it comes to print materials, past research demonstrates that the appearance of written educational pieces for the ageing population is important (Lancaster *et al.*, 1997). It has been shown that some features in the appearance of an educational piece are integral in enticing the elderly to pick up a piece, while other features are important to maintain interest. Three characteristics emerged to determine whether a piece would be picked up. Print size (Palatino 14), along with white space, were important. The comment, 'There's not so much print to read through … less confusing and congested,' reflected the preference for white space. The content of the piece as reflected in the title was also found to be important as reflected in the statement, 'I'd pick up this first because of the word 'quick' or 'safe' in the title' and 'I'd pick up Using a Meat Thermometer first because it's almost Thanksgiving' (Gettings and Kiernan, 2001).

On the other hand, four characteristics emerged as key attributes in determining what piece they liked the best. Content and amount of content were considered vital by the groups. 'It has everything in it you need to know, and there's a great deal of references,' reflects the desire for a considerable amount of content. The format of the piece also carried weight as suggested by the comment, 'I can place the pamphlets with my recipes and cookbooks and the three-fold brochure in my pocket or purse.' In an addition, the groups would like to see pictures of family members of various ages, including older individuals, depicted in the educational piece (Gettings and Kiernan, 2001).

24.3.4 Motivation to come to programs

Since programs are one of the delivery methods preferred by the elderly, research shows that this group is motivated to attend a program with an educational focus. When marketing the program, they suggested advertising that new information is featured. This is reflected in the statement, 'Just tell us that we will learn new ideas and techniques for food safety.' Another motivating factor is incentives like a meal, but do not interrupt bingo or parties. The presence of a special person, i.e. volunteer or surprise speaker, is also a motivating factor to attend a program. When asked what would prevent them from attending a program about food safety, they stated other activities occurring at the same time and the attitude that they don't need to learn (Gettings and Kiernan, 2001).

Because the ageing population considers physicians and their offices to be preferred methods of receiving food safety education, it is important that physicians recognize and treat foodborne illness and educate patients in proper food-handling practices.

It has been suggested that physicians who see patients with acute gastroenteritis consider foodborne pathogens as a possible source of infections and should consider themselves as critical sources of food safety information for their elderly patients (Kendall *et al.*, 2006). If a person seeks treatment for gastroenteritis, it is common for physicians not to consider it as food or hygiene related, which results in an underestimate of the true incidence of foodborne illness throughout the world. Many physicians and other health care professionals view a stool culture as an unnecessary expense since the results may not be available in time to decide on a treatment (Mead *et al.*, 1999; Wheeler *et al.*, 1999). However, the CDC document *Food Safety for High Risk Populations* states each stool culture with positive results may represent the sentinel case of a foodborne illness in a more widespread outbreak. Guerrant and colleagues (2001) recommend that any diarrheal illness lasting more than one day should result in the prompt evaluation of a fecal specimen, especially if it is accompanied by a fever, bloody stools, systemic illness, recent use of antibiotics, day-care attendance, hospitalizations, or dehydration. Without a stool culture to confirm a specific diagnosis, patients are more likely to receive inappropriate treatment and potentially worsening the course of their illness or facilitating the emergence of antibiotic resistance of a pathogen (Guerrant *et al.*, 2001).

Due to the fact that physicians and other health care professionals can be integral in the prevention and control of foodborne illness, two resources are available. The American Medical Association, the American Nurses Association, and several other government agencies developed a teaching tool entitled *Diagnosis and Management of Foodborne Illness: A Primer for Physicians and Other Health Care Professionals* (CDC, 2004). A second educational tool, CDC's *Food Safety for High Risk Populations*, (http://hec.osu.edu/highriskfoodsafety) is a six-module online continuing education course examining the immune system and why the elderly, as one of the high risk groups, is at greater risk.

24.4 Future trends

According to FoodNet figures, 80% of the United States population consumes food prepared outside the home at least one time per week. The data also reveals this pattern of consumption is associated with increased risk of foodborne illness (Jones *et al.*, 2002).

As the population ages, so will the need for services to address their needs. Two areas that will continue to grow with the ageing population are nursing home care and home-delivered meals (Fey-Yensan, 2001), both of which are critical to the future safety of the ageing population.

It is estimated that 5% of people over the age of 65 and 20% of people age 85 and older reside in nursing homes. Besides the underlying causes of foodborne illness in the elderly that have previously been elaborated upon, the close confinement of those living in nursing homes also increases their vulnerability to a foodborne illness (Buzby, 2002).

Foodborne disease outbreaks occurring in nursing homes result in severe consequences. Between 1975 and 1987, the case-fatality for foodborne outbreaks due to *Campylobacter* associated with nursing homes was 1%, which is ten times the 0.1% case-fatality rate for foodborne outbreaks at other sites (Buzby, 2002; Gerba *et al.*, 1996; Levine *et al.*, 1991). Death was especially at higher rates for *Salmonella* species, staphylococcal foodborne disease, and *E.coli* O157:H7. In addition, deaths as a result of infection from *Campylobacter* species and *Clostridium perfingens* occur at increased rates in nursing homes. In fact, from 1993–1997, *Morbidity and Mortality Weekly Report* (CDC, 2004) reveals 40% of deaths from *Salmonella enteritidis* were nursing home residents.

Home-delivered meals, funded by the Older Americans Act, reach more than 875,000 elderly citizens each year who are functionally or medically unable to shop and/or prepare foods for meals. It is estimated that 41% of Elderly Nutrition Programs have waiting lists for home-delivered meals (Ponza *et al.*, 1996). Research has shown that saving portions of home-delivered meals for consumption later in the day is common (Fogler-Levitt *et al.*, 1995; Lau *et al.*, 1994; Asp and Darling, 1988). In fact, Asp and Darling (1988) reported as many as 50% of those who received meals saved food for later in the day. Lau and colleagues study (1994) revealed that only 12% (48) of more than 400 home-delivered meal recipients consumed the meal in its entirety. A study by Fey-Yensan *et al.* (2001) discovered 82% (189 of 230) of Meals-On-Wheels recipients from Rhode Island were found to be at high nutritional risk, which then increased their risk of a foodborne infection. Food safety concerns were reported for 26% (61 of 230) of the meal recipients. Participants who did not eat their entire meal upon arrival were more likely to be older clients (75 years of age and above), women, participating in the program for one to two years, receiving social security benefits, and at highest nutritional risk. Of those who stored all or part of their meal, 30% (169) stored it on the counter, at prime temperature for bacterial growth.

Issues in the food service industry, such as high turnover and level of education for line employees, make it difficult to maintain employees and

volunteers trained in proper food-handling practices. who work and volunteer in restaurants, nursing homes, and organizations preparing home-delivered meals.

Another trend affecting food safety in the ageing population deals with the globalization of the food supply. As the food chain becomes more complicated, the consumer has a greater role to play in ensuring the safety of food. While the globalization of the food supply is introducing an ever increasing variety of new foods to our local markets and restaurants, it is also introducing new food pathogens into the food system (Bender *et al.*, 1999). Seafood and fresh fruits lead the list of imported commodities, both of which can be vehicles for foodborne pathogens (Cohn, 2001). Examples of foodborne illness/outbreaks associated with globalization of the food supply were the 1996 North American outbreak linking raspberries from Guatemala to cyclosporiasis (Herwaldt and Ackers, 1997) and *Salmonella typhi* infection in Florida linked to frozen mamey produced in Guatemala and Honduras (Katz *et al.*, 2002). The US FDA, as authorized by the 1997 FDA Modernization Act, works with other countries and international agencies to prevent foodborne illness (Cohn, 2001). In addition, the US FDA (2001a) established and promulgated procedures and rules to prevent contaminated foods from being marketed in the United States. In the year 2000, this organization's programming and initiatives related to food safety involved over 30 nations.

Other areas of food safety that should at least be mentioned are food bioterrorism, food biotechnology, and irradiation. While these may not be areas in which the ageing population can have a direct influence, they should be considered when talking about the safety of food, since they are a part of our world and/or our food supply.

In the past, food has been used to inflict harm and influence politics (Grossman, 2001) and could be used again by terrorists. The role of the consumer will be critical in a food bioterrorism act since the general public will likely be the first to be targeted. (Peregrin, 2002) The Public Health Emergency Preparedness and Response – Biological diseases/agents document developed by the CDC has targeted several foodborne pathogens as having the potential to cause harm. These include tularemia; brucellosis; Clostridium botulinum toxin; the epsilon toxin of *Clostridium perfringens*; and infection with *Salmonella*, *E.coli*, and *Shigella*. Due to the centralized nature of food production and processing and the wide distribution of foods, the CDC believes the food sector is vulnerable to attack (Sobel *et al.*, 2002). Cramer (2001) reports the food industry has recognized the potential for bioterrorism and has developed guidelines to aid in thwarting an attack.

A great deal of controversy has surrounded the topic of biotechnology (genetic engineering) and food irradiation. The Institute of Food Technologists *Expert Report on Biotechnology and Foods* documents the potential problems with genetically modified foods to include allergenicity and expressions of either toxicity or antinutrient effects. The report also cites a National Research Council Report (2000) which stated the assessment of genetically engineered foods should focus on a food's property, such as protein content and content of

other substances, rather than on the genetic alteration process itself. The role of consumers, especially for those who have allergies, will be to determine whether they choose to purchase these products.

According to the CDC's *Frequently asked questions about food irradiation*, this process exposes food to ionizing radiation to kill foodborne pathogens and has been used to treat raw meat and poultry to destroy *E. coli* O157:H7, *Salmonella*, and *Shigella*; ready-to-eat meats to destroy *Listeria monocytogenes*; produce to reduce *Cyclospora*, *Shigella*, and *Salmonella* (CDC)

The CDC also indicates that nutrients in food are not substantially changed by irradiation except for a slight reduction in the thiamin content. Because irradiated foods are not free from pathogens, the consumers' role is to follow proper food-handling practices to inhibit bacterial growth as they would if foods were not irradiated.

24.5 Conclusions

There are many issues that need to be addressed in the area of food storage and preparation practices among the elderly. In the food storage area, it is necessary to educate the ageing population of the appropriate refrigerator temperature of 41 degrees Fahrenheit or lower to inhibit bacterial growth in stored foods. Research has not studied the amount of time that food remains in refrigerated storage after it is brought home from the grocery store, cooked, or delivered. This is an area that should be studied and included as part of an educational endeavor with the elderly.

In the food preparation arena, improper thawing practices and thawing in refrigerators with a temperature above 41 degrees Fahrenheit is prevalent. Using a thermometer to determine whether foods are cooked adequately is necessary for small pieces not just large cuts of perishable foods. Cooling foods by taking large quantities and portioning them into smaller quantities must be emphasized to the ageing population to reduce the incidence of foodborne illness.

While barriers such as old habits, lack of resources, and inconveniences are reported by those who do not follow safe food storage and handling recommendations, the ageing population is agreeable to change their inappropriate practices. They want credible information from credible sources. Since physicians are listed as a credible source, it is essential that they recognize and treat foodborne illness and educate patients in proper food-handling practices.

Delivery of food safety messages to this group poses a great challenge. The ageing population wants to be convinced that there is a real threat to their health when participating in unsafe practices. Educators have many methods (written pieces, videos and programs) and venues to educate this population, including home and in central locations, like senior centers. When developing educational materials, it will be imperative to understand the current research as to what is appealing to this group as well as conduct focus groups to evaluate these materials.

As the ageing population and their experiences change, continued research in this area is necessary. While the majority of studies have involved focus groups, more large-scale studies are necessary so that recommendations can be generalized. Governments and food manufacturers must continue to work together to enhance policy to reduce the incidence of foodborne illness in the ageing population. Based on current research, an area that should be addressed is the print size of 'use-by,' 'sell-by,' and 'best-by' dates on food packages. This has been studied in the UK and should be addressed by government agencies in all countries to help the ageing population, with typically poor eyesight, to be able to more easily read these dates on packages (Johnson *et al.*, 1998). Policy should address including instructions on food packages for proper storage, thawing, cooking, and cooling.

With 80% of the United States population consuming food prepared outside the home at least one time per week (Jones *et al.*, 2002), 5% of people over the age of 65 and 20% of people age 85 and older residing in nursing homes (Buzby, 2002), and more than 875,000 elderly citizens receiving home-delivered meals, proper food safety training of food service personnel and/or volunteers in nursing homes, the Meals on Wheel program, and in all restaurants is an area than cannot be overlooked. There are several well-respected certification programs available (see resources). To meet the needs of volunteer education, Penn State Cooperative Extension has developed a food safety training curriculum to address their needs. The Cooking for Crowds curriculum focuses on basic food-handling procedures and how to deal with volunteers, who believe because they have been preparing food for a long time, they know the safest ways to handle foods. In addition, for those families and care-givers of the elderly, they too need to receive consumer food safety education.

Hudson (2002) and colleagues concluded their research with the suggestion that food safety professionals need to empathize, develop a discourse that does not sound patronizing, and promote equal responsibility for a safe domestic environment. They believe most consumers are receptive and willing to accept responsibility for ensuring that the food they eat is safe.

Focus group findings reveal that food safety advocates need to address specific belief facilitators, such as tradition, skepticism, habit, and media exposure in combating improper food handling behaviors. Further research is needed into communication avenues, methods, and timelines to provide effective messages to correct inappropriate food handling practices (Boone *et al.*, 2005).

The Healthy People 2010 food safety project, co-lead by the FDA and the United States Department of Agriculture's Food Safety Inspection Service, have targeted specific objectives to reduce foodborne illness by the year 2010. Those that have been addressed here include:

- reduce infections caused by key foodborne pathogens
- reduce outbreaks of infections caused by key foodborne bacteria
- increase the proportion of consumers who follow key food safety practices

- improve food employee behaviors and food preparation practices that directly relate to foodborne illness in retail food establishments.

Food safety information is abundant and available to the ageing population in the United States, Europe, and Australia (see list of educational references). It is the responsibility of health care professionals and educators to address these issues with this at-risk population using the best research that we have.

24.6 Sources of further information and advice

- US Dept. of Agriculture's (USDA's) Food Safety Inspection Service
  http://www.fsis.usda.gov/
- USDA's Food Safety Research Information Office
  http://fsrio.nal.usda.gov/index.php
- USDA's Fight Bac Campaign
  www.fightbac.org
- US Food and Drug Administration's (FDA) Center for Safety and Applied Nutrition
  http://www.cfsan.fda.gov/list.html
- US Centers for Disease Control (CDC) and Prevention Food Safety Office
  http://www.cdc.gov/foodsafety/
- CDC's National Center for Infectious Disease
  http://www.cdc.gov/ncidod/diseases/food/safety.htm
- CDC's Diagnosis and Management of Foodborne Illnesses: A Primer for Physicians and Other Health Care Professionals
  http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5304a1.htm
- CDC's Food Safety for High Risk Populations
  http://hec.osu.edu/highriskfoodsafety/
- US Dept. of Health and Human Services
  http://www.healthfinder.gov/scripts/SearchContext.asp?topic=321
- Gateway to Government Food Safety Information
  http://www.foodsafety.gov/
- Penn State Cooperative Extension Food Safety Home Page (educational curriculum for food service employees, volunteers, food processors and manufacturers, and the public)
  http://foodsafety.cas.psu.edu
- University of Nebraska Cooperative Extension in Lancaster County
  http://lancaster.unl.edu/food/links.htm
- Colorado State University Food Safety for High Risk Groups
  http://www.colostate.edu/orgs/safefood/foodsafety/menuhr.html
- American Dietetic Association's Home and Food Safety
  http://www.homefoodsafety.org/index.jsp
- American Association of Retired Persons
  http://www.aarp.org/health/staying_healthy/eating/a2003-03-10-foodsafety.html

- World Health Organization
  http://www.who.int/topics/food_safety/en/
- Codex Alimentarius
  http://www.codexalimentarius.net/web/index_en.jsp
- Institute of Food Technologists
  http://www.ift.org/cms/
- UK Food Standards Agency Safety and Hygiene
  http://www.food.gov.uk/safereating/
- Australian New Zealand Food Authority
  http://www.nzfsa.govt.nz/about-us/
- Australian Food Safety Centre of Excellence
  http://www.foodsafetycentre.com.au/
- Australian Government Initiative Health Insititute
  http://www.healthinsite.gov.au/topics/Food_Safety
- Australian Food Safety
  http://www.safefood.net.au/Safe+Food.htm
- Food Science Australia Food Safety and Hygiene
  http://www.foodscience.csiro.au/fshlist.htm
- Australian Food Safety Council
  http://www.foodsafety.asn.au/contactus.cfm
- European Food Safety Authority
  http://www.efsa.europa.eu/en/about_efsa.html
- European Food Information Council
  http://www.eufic.org/
- European Association for Food Safety
  http://www.safeconsortium.org/
- WHO Regional Office for Europe Food Safety Home Page
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25

Developing nutrition education programs for older people

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Knowing is not enough; we must apply.
Goethe

Abstract: Information on the nutritional needs of older adults has outpaced education. There is a lag between knowledge acquired and the transmission of this knowledge to the target population. In this chapter, we explore this issue and present components of successful nutrition intervention programs that may have contributed to their success. We offer a theoretical framework that is based on the ecological model and includes features thought to increase the effectiveness of nutrition education programs. This framework can serve as a guideline for designing future nutrition interventions.

Key words: aging, lifestyle, nutrition education, nutrition intervention, older adults, theoretical framework, translational research, trends.

25.1 Introduction

It is well recognized that proper nutrition is crucial to maintaining good health, preventing or delaying the most common chronic diseases, and managing such diseases. In the US, the 'Dietary Guidelines for Americans' is a policy document that is updated every five years and that presents evidence-based recommendations for a healthy diet. These nutrition recommendations target the general population and include consuming several servings of fruit and vegetables per day, eating whole grains, and limiting intake of sodium and saturated fatty acids. However, at every stage of the life cycle, including advanced age, physiological changes occur which place additional demands on the body and modify dietary requirements for health. Older adults who have maintained a healthy diet

throughout life are still thought to have increased requirements for nutrients such as vitamin D and calcium, for example.

The body of knowledge on the nutritional needs of older adults has been growing rapidly over the past 20 years. In 1997, the Food and Nutrition Board split the oldest age category of the Dietary Reference Intakes, 50 years and older, into two categories, 50–70 and 71 and over. This change stemmed from the growing body of knowledge on older adults and the recognition that nutrient needs of the older age group differ from those of the younger age group.

Information on the nutritional needs of older adults has outpaced education. There is a lag between knowledge acquired and the transmission of this knowledge to the target population. Older adults have been largely ignored by initiatives for health promotion and disease prevention and by clinical trials for a number of reasons. There is a general misconception that older adults are resistant to change. Evidence is accumulating, however, that older adults are more successful at changing their diets than younger adults (Wing *et al.*, 2004; Whelton *et al.*, 1998). In the Diabetes Prevention Program (DPP), funded by the National Institutes of Health (NIH), individuals at high risk of developing diabetes were randomly assigned to one of three groups; a control group, a metformin (oral glycemic control drug) therapy group, or an intensive lifestyle intervention group (Wing *et al.*, 2004). The lifestyle intervention consisted of 7% weight loss, achievement or maintenance of at least 150 minutes of moderate physical activity per week and a reduction of total dietary fat to less than 25% of calories. Results showed that older age was a strong predictor of success at meeting the weight loss and physical activity goals and at reporting a lower percentage of calories from fat. The highest achievers were those age 65 and older. Because older adults were more likely to adhere to multiple components of the lifestyle intervention and to complete self-monitoring records, the authors suggested that older adults appear particularly good candidates for lifestyle interventions. Similarly, results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE) indicated that older patients with hypertension were able to make and sustain lifestyle changes (Whelton *et al.*, 1998). While many studies have shown higher rates of success among older adults, the Women's Health Initiative (WHI) study did find that compliance with dietary modification was lower among adults age 65 and older than among those age 50–64 (WHISG, 2004).

Another barrier to funding studies which include older adults is the belief that chronic disease is an outcome of lifelong lifestyle choices and that making dietary changes later in life does not influence morbidity and mortality. In 2003, men in the US who survived to age 65 years had on average 16.8 years remaining to live and women 19.8 years. Chronic diseases and conditions such as arthritis, diabetes and heart disease, as well as disabilities that result from injuries such as falls, do develop later in life. Older Americans are disproportionately affected by these conditions which limit activities and account for seven out of every 10 deaths and more than three-quarters of all health care expenditures in the US. Although it is recognized that nutrition education should

begin early in life, the question remains about whether a healthy diet can help maintain functional independence among healthy older people, prevent illnesses among older people with chronic disease and help maintain function among frail older adults. Studies have shown that primary and secondary prevention interventions can be effective among older adults. In a scientific statement, the American Heart Association subcommittee on Exercise, Cardiac Rehabilitation and Prevention reported that secondary interventions to modify risk factors in older patients with coronary heart disease (CHD) were as effective as in younger adults (Williams *et al.*, 2002). In addition, lifestyle intervention studies in older adults have shown improvement in biochemical markers. For example, in the TONE study which examined the effect of lifestyle modification on hypertensive adults 60–80 years old, sodium reduction, weight loss, and the two combined reduced the need for blood pressure medication by 31%, 36% and 53%, respectively (Whelton *et al.*, 1998). Also, rates of cardiovascular problems were lower in the intervention groups versus the control group. Another study which examined the impact of lifestyle intervention on obese older adults showed that those who lost weight and exercised lowered CHD risk factors including C-reactive protein, free fatty acids and interleukin 6, and also had a lower incidence of the metabolic syndrome (Villareal *et al.*, 2006).

Other limitations in the transference of nutrition knowledge to older adults include the difficulty in measuring outcomes in nutrition interventions. Nutrition interventions are usually multifaceted, and their pathways to impact are complex. Among older adults in particular, afflictions from chronic diseases may obscure relationships between interventions and outcomes.

Finally, the US has historically given priority to funding basic research and treatments for disease rather than funding prevention programs. Basic research on aging has not resulted in practical applications that benefit older adults. However, with the surge in the number of older adults and concern over rising medical care expenditures, research priorities are shifting towards prevention of chronic diseases.

25.2 Translational research

As evidence of the role of nutrition in health grows, there is increased attention to nutrition interventions to prevent chronic diseases among older adults. In the NIH roadmap which lays out research priorities for the future, the research plan promotes translational research, defined as 'the application of discoveries from basic biomedical and behavioral research toward the diagnosis, treatment or prevention of human disease, with the ultimate goal of improving public health' (National Institutes of Health, 2007b). In other words, basic scientific discoveries must be translated into practical applications (Fig. 25.1). To date, there are few randomized controlled studies which have examined the impact of lifestyle interventions, including nutritional, on disease outcomes in older adults. Even fewer studies have examined the effectiveness of nutrition interventions

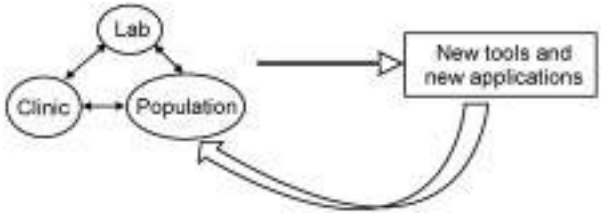

Fig. 25.1 Translational research diagram. Source: National Cancer Institute.

and their impact on long-term health among older adults at the community level, in 'real-life' situations. However, these types of studies, also known as evidence-based nutrition programs (EBNP), are increasing.

25.3 Evidence-based nutrition programs (EBNP)

Due to budgetary constraints, there has been a major drive towards identifying and replicating EBNP nationwide in the US. Evidence-based public health (EBPH) is defined as the process of integrating science-based interventions with community preferences to improve the health of populations (Kohatsu *et al.*, 2004). EBNP are interventions that have been clinically tested and then taken from their controlled experimental settings to large communities or populations. The Administration on Aging, an agency of the Health and Human Services in the US, has provided grant opportunities to states to support the implementation of evidence-based disease and disability prevention programs for older adults at the community level. These programs are administered at the community level through non-profit aging service providers, such as senior centers, nutrition programs, senior housing projects and faith-based organizations, which work with seniors in their own communities to help them adopt lifestyle and behavioral changes that can improve the quality of their lives.

Despite the drive to fund and administer such programs, there are few practice-based nutrition interventions that have been tested and validated at the community level. Many published studies have tended to use convenience samples, be of short duration and have limited market segmentation. Few studies have stated their specific objectives, or have many measured outcomes. However, these interventions can be used as a basis for future programs.

The following section presents salient components of different studies which may have led to successful outcomes. A review of some smaller-scale studies was published previously (Sahyoun *et al.*, 2004). The following section focuses on larger studies, in particular from the last five years. Due to multiple intervention components, it is not possible to determine which of these may have led to study outcomes; however, reasonable assumptions and common sense indicate the potentially successful features of these studies.

25.4 Developing nutrition education programs for older adults

Effective nutrition intervention programs for older adults share features that can be incorporated into future interventions to increase their chance of success. These include tailoring objectives to individuals' needs and interests, involving participants in setting goals, monitoring results, providing clear and practical messages, offering frequent access to well-trained health professionals, acknowledging outside influences on individuals' dietary choices, and using appropriate theories of behavioral change in the program design (Sahyoun *et al.*, 2004).

25.4.1 Individualized goals

Interventions that are customized to each participant have shown a high rate of success. Miller *et al.* (2002) significantly improved glycemic control of older adults with type 2 diabetes through a nutrition education program tailored to individuals' needs. In a brief dietary intervention, Constans *et al.* (1994) increased calcium intake of older adults to at least 800 mg/day by providing suggestions based on each subject's taste preferences and baseline calcium intake.

While it may be a challenge to personalize an intervention on a large scale, several effective large-scale interventions have customized their messages. Campbell *et al.* (1999) increased fruit and vegetable consumption of African-American church-goers by providing personalized messages based on participants' current fruit and vegetable intake, cultural background, personal beliefs and sources of social support. In the Trial of Nonpharmacologic Interventions in the Elderly (TONE) to reduce sodium intake and decrease weight if appropriate, participants were assisted in adapting program recommendations to their personal circumstances, and individual progress was closely monitored (Whelton *et al.*, 1998).

The Women's Health Initiative (WHI) Dietary Modification Trial achieved a 10% lower intake of energy from fat by adapting goals to participants' current diets, needs and interests (WHISG, 2004; Patterson *et al.*, 2003). Similarly, the Diabetes Prevention Program (DPP) lifestyle intervention, which reduced the risk of type 2 diabetes by 58% through diet and physical activity, acknowledged the cultural heterogeneity of its cohort and was designed to be as flexible as possible to meet each individual's needs (Diabetes Prevention Program, 2002). A case manager or 'lifestyle coach' helped identify specific barriers to dietary adherence and develop a personalized toolbox of adherence strategies (DPP, 2002). In the Finnish Diabetes Prevention Study (DPS), which also lowered risk of diabetes by 58%, a nutritionist tailored dietary advice to each subject's needs, interests, level of education, and personal challenges (Eriksson *et al.*, 1999). At the same time it was recognized that group sessions could foster more social support for participants than individual meetings, and that a combination of individual and group sessions may be optimal (Lindstrom *et al.*, 2003).

Computer programs can personalize nutrition education programs even at the population level. The MyPyramid website released by the USDA includes

interactive tools that customize its recommendations to each person according to age, gender and level of physical activity (King, 2007). These tools allow people to design their own food intake plans and guide them in following the plans (King, 2007). In a smaller computer-assisted intervention, Stevens *et al.* (2003) significantly increased adults' intake of fruit and vegetables and lowered their fat consumption. Participants answered questions through a touch screen computer system about their current diets, willingness to change their diets and personal barriers to change, and materials were customized based on responses (Stevens *et al.*, 2003).

Personalized telephone-based interventions have also shown some success among a highly motivated, breast cancer survivor cohort. In the Women's Healthy Eating and Living (WHEL) study, telephone counseling produced a significant increase in vegetable intake (by 3.2 servings per day) and in fruit intake (by 0.6 servings per day) (Pierce *et al.*, 2004). Recommendations were tailored to participants based on their current diets, personal barriers to change, and level of self-efficacy related to planned dietary changes (Pierce *et al.*, 2004).

25.4.2 Participant involvement

Interactive interventions can be more effective than those without participant involvement in setting goals and monitoring results. The WHI considered self-management a key strategy for achieving and maintaining dietary changes, as did the DPP (DPP, 2002; NIH, 2007a). In the WHI, participant input led to the development of new self-monitoring tools and quarterly newsletters (WHISG, 2004). DPP participants were taught self-monitoring skills and were provided food scales, measuring utensils and booklets that allowed them to track calorie and fat intakes (DPP, 2002). In the DPS, subjects devised intermediate goals for themselves (Lindstrom *et al.*, 2003). Also, in the intervention by Stevens *et al.* (2003) participants identified their own strategies to overcome barriers to achieving their goals.

25.4.3 Intensive program

An aggressive approach, especially at the start of an intervention, may be important for its long-term success. Campbell *et al.* (1990) compared an intensive program to a conventional program to achieve a fat intake of $\leq$30% and a carbohydrate intake of $\geq$50% of total energy in adults with uncontrolled type 2 diabetes, and found that the intensive approach yielded significantly greater dietary compliance. The WHI included 18 group sessions in the first year, and quarterly sessions in subsequent years (WHISG, 2004). In the DPP, the initial core curriculum was the most intensive, and participants' ability to meet intervention goals in the short term strongly predicted their long-term adherence (DPP, 2002). The DPS also sought to provide the most intensive intervention in the first months, and each participant had an average of 20 dietary counseling sessions overall (Eriksson *et al.*, 1999; Lindstrom *et al.*, 2006). The TONE

intervention had an initial four-month intensive phase, which imparted core knowledge and behavior skills (Whelton *et al.*, 1998).

25.4.4 Clear objectives

Clearly defined, simple and practical objectives are a common feature of effective intervention programs. Campbell *et al.* (1990) strove for extreme simplicity in their dietary instruction, and considered this an optimal means of promoting adherence. Constans *et al.* (1994) had the sole goal of increasing participants' calcium intake to at least 800 mg/day. The Black Churches United for Better Health Project also had a single objective of increasing fruit and vegetable consumption by at least ½ serving per day (Campbell *et al.*, 1999). The WHI (2004), DPP (2002) and DPS (Lindstrom *et al.*, 2003) all provided straightforward and practical dietary and weight loss goals, and introduced only one message at a time to participants. The WHEL intervention also focused on providing easily understandable behavioral goals to help women achieve a healthful dietary pattern (Pierce *et al.*, 2004).

25.4.5 Appropriately-trained health professionals

Interventions that are delivered by well-trained health professionals, including nutritionists, behavioral psychologists and physicians, are believed to have the greatest impact. Professionals with expertise in the specific nutritional and behavioral components of the intervention are considered to be best suited to tailor the program to individuals and guide them in changing their dietary behavior (Miller *et al.*, 2002). In the TONE study, nutritionists and exercise counselors with experience in lifestyle change techniques delivered the intervention (Whelton *et al.*, 1998). The DPP was developed and implemented by a range of highly-qualified health professionals, and case managers who typically had at least Master's degree training in behavioral psychology, health education or exercise physiology (DPP, 2002). Master's degree-level health counselors also implemented the intervention designed by Stevens *et al.* (2003).

Similarly, the DPS employed well-qualified nutritionists, physicians and other health care professionals, and WHI nutritionists and WHEL dietary counselors were trained in behavioral theory (WHISG, 2004; Lindstrom *et al.*, 2003; Pierce *et al.*, 2004). Another successful diet and physical activity intervention which decreased multiple metabolic risk factors in obese older adults was led by a dietitian with specific experience in group behavioral therapy for obesity (Villareal *et al.*, 2006).

25.4.6 Access to health professionals

Easily accessible health professionals play a major role in successful nutrition intervention programs. In the DPP, lifestyle coaches were encouraged to meet with participants as often as necessary to sustain adherence to the program (DPP,

2002). Frequent contact with health professionals was also a key feature of the DPS, and the WHEL study involved regular telephone contact with dietary counselors (Eriksson *et al.*, 1999; Pierce *et al.*, 2004).

25.4.7 Attention to social and physical environment

Programs that acknowledge the importance of outside influences on individuals' dietary behavior and that target multiple levels of change appear to have the most impact on behavior change (Institute of Medicine, 2001). Campbell *et al.* (1999) used an ecological framework to increase fruit and vegetable intake, and targeted not only individuals, but their social networks and communities, including local grocery stores. Institutionalization of the program within the structure of the church ensured longer-term dietary adherence. The WHI also recognized the 'critical nature of social influences on eating and on successful health behavior change,' and included social support as a central theme (NIH, 2007a; Kearney *et al.*, 2002). In the WHI, problem-solving was conducted as a group effort, and participants involved significant others in their process of dietary change (NIH, 2007a). Similarly, in the DPS, if the person primarily in charge of preparing meals in the family was not the study subject, this person was invited to join the sessions (Eriksson *et al.*, 1999).

25.4.8 Use of theories of behavioral change

Theory-based interventions seem to have an increased likelihood of positive results. Behavior change theories explain the dynamics of behavior, the processes for changing behavior and the effects of external influences on behavior. They are behavioral maps to better understand, and therefore predict, behaviors. These theories identify the most suitable targets for intervention programs, the methods for accomplishing change and the outcomes to evaluate.

Miller *et al*. (2002) incorporated multiple behavioral theories into their intervention to improve knowledge of the food label, and attributed their success to this theory-based approach. Campbell *et al.* also assimilated concepts from several behavioral theories to increase fruit and vegetable consumption of participants. Other successful interventions have strongly relied on behavioral theories, including Social Cognitive Theory, which proposes that behavior is influenced by continuous interaction among the environment, an individual's characteristics, including knowledge, skills, and health beliefs, the behavior itself, and results of the behavior (Whelton *et al.*, 1998; Campbell *et al.*, 1999; Patterson *et al.*, 2003; Stevens *et al.*, 2003; Pierce *et al.*, 2004; NIH, 2007a). In the DPP and DPS, participants were taught behavioral strategies to achieve long-term changes in their fat and calorie intakes, and in the study by Villareal *et al.*, subjects participated in weekly behavioral therapy group meetings (Villareal *et al.*, 2006; DPP, 2002; Eriksson *et al.*, 1999).

25.4.9 Incentives

In the Diabetes Prevention Program DPP (2002), participants received small incentives such as t-shirts, newsletters, and other materials to encourage them to maintain positive behavior changes. In addition, $100 was available per participant per year for incentives such as cookbooks or grocery store vouchers. Several smaller-scale studies also found that providing incentives likely encouraged dietary change and decreased rates of attrition (Sahyoun *et al.*, 2004).

25.5 A framework for nutrition intervention

A theoretical framework based on the ecological model and modified from a previous version is presented in Fig. 25.2. The framework is a graphic representation of the features that are believed to potentially contribute to the success of nutrition education programs and includes the characteristics described above. This framework can be used as a guideline for designing future nutrition interventions for older adults. Intervention features which target the individual include developing clear and practical objectives which are tailored to the profile of the target population. The messages must also reflect these objectives and be culturally and ethnically sensitive. Other potentially successful components include providing easy access to dietitians and other health professionals, motivating participants to determine their own project goals and to monitor results, and using incentives. Additional components derived from more recent studies have been incorporated into the framework. These include creating support groups, involving family members in the intervention and enlisting support of local grocery stores.

This framework will evolve as additional features are incorporated into interventions and found to potentially contribute to their success. However, in the future, it is recommended that individual study components be tested in order to get a better grasp of what works and in which setting.

The framework also includes evaluation components as a reminder of their importance. Formative research in the initial phase of an intervention is necessary to match participants' needs with program objectives and to provide additional knowledge on the social and cultural issues that need addressing. An intervention that works well in one setting may be ineffective elsewhere, and adapting educational messages to population characteristics is crucial. Additionally, process evaluation is needed to determine whether the intervention was delivered and received as intended. Such measures may include assessment of attrition rates and adherence. Another critical factor is to determine appropriate outcome measures that will assess change in behavior as a result of the intervention. Research to identify biomarkers and other appropriate outcome measures is ongoing.

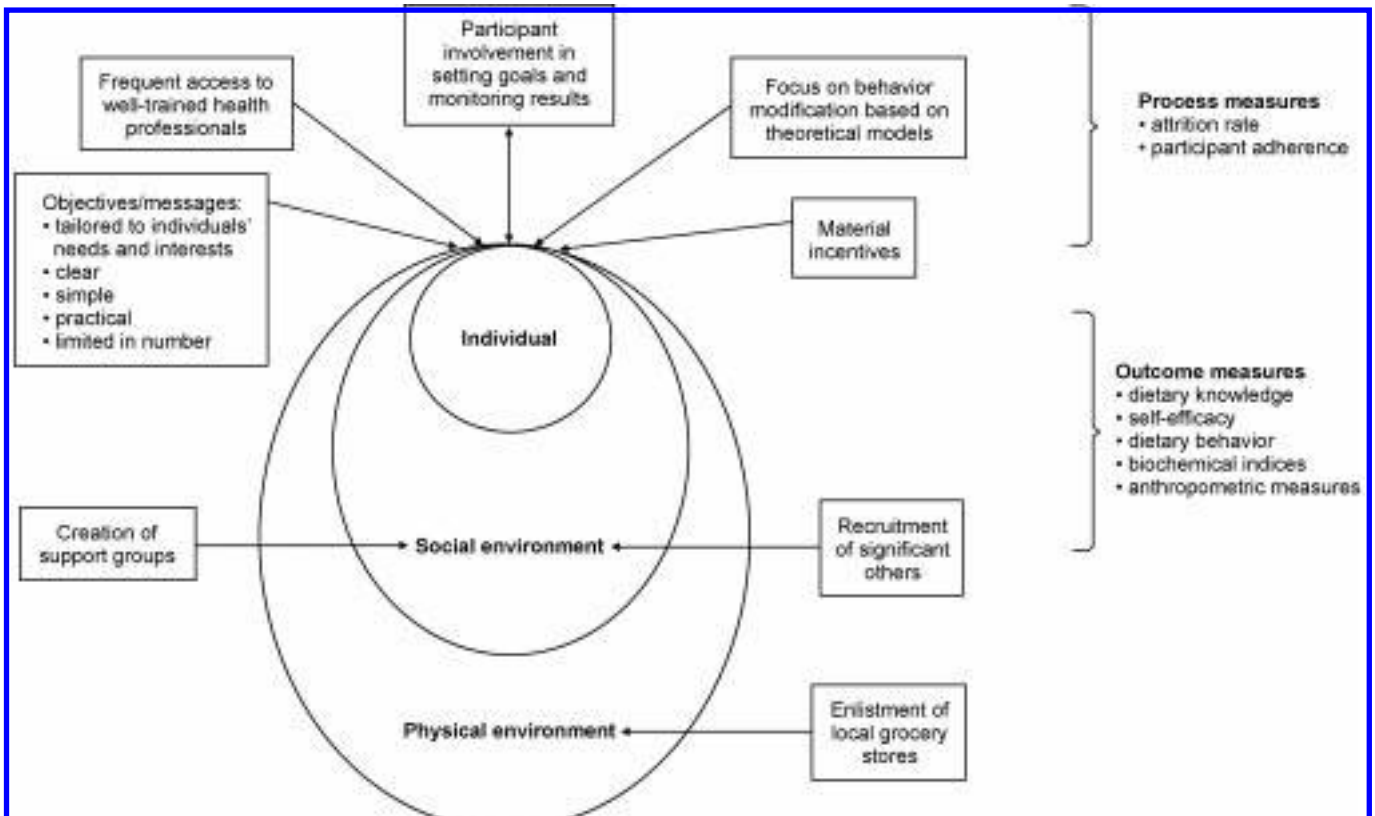

Fig. 25.2 A framework for designing a nutrition education intervention for older adults.

25.6 Future trends

The next generation of older adults, also known as the baby boomers, is expected to be healthier, wealthier, more health conscious and possibly more politically savvy. They will most likely demand from governments and communities more programs to assist them in maintaining health and function. In addition, due to the increase in interest in complementary and alternative medicine, there may be a more holistic approach to health whereby greater attention will be placed on environmental and social factors and their impact on health and quality of life. There is a growing responsibility to translate the tremendous new scientific discoveries into public health programs that take into consideration the growing needs of the older adult population and ensure more health gains for the nation.

To be successful in reaching the targeted audience, more information is needed on dietary behavior of consumers and a better understanding of the factors that go into decision making regarding food selection and health behavior. Adapting theories of behavior change in nutrition interventions is a wonderful enrichment of the field of nutrition education and promises interesting interdisciplinary effort between nutritionists and behavioral scientists.

Another area of tremendous potential that will add another dimension to nutrition education is the field of genomics, which examines an individual's total genetic makeup as well as interactions of genes with each other and with the person's environment. The first phase of the Human Genome Project was completed in 2003, and researchers can now investigate thousands of variations in human genes in relation to individuals' nutritional needs for optimal health (CDC, 2007). Findings could allow nutrition interventions for older adults to be tailored to participants' genetic characteristics and thus to become even more personalized (Stover, 2006).

One nutrition message may not fit all, which is perhaps a reason for the discrepancy in health outcomes obtained from intervention studies on different population groups. To date, variations in multiple genes have been shown to influence nutrient metabolism and nutritional needs. Variations in genes for proteins involved in the metabolism of vitamin B12 and of vitamin D appear to affect requirements for these two nutrients of importance to older adults (Stover, 2006). While it may take decades before effects of genetic variation on nutritional requirements are fully understood, due to the volume and complexity of genomic information, continued intensive research in nutritional genomics is justified. Appropriate interventions which tailor dietary recommendations to individuals' genomes have the potential to save billions of dollars in health care costs and to substantially increase the health and well-being of older adults as well as other subgroups of the population (Collins and Manolio, 2007).

An additional trend is the increasing use of computer technology and the world wide web, which can allow interventions to be individualized even at the population level. The MyPyramid website, for example, tailors national dietary

recommendations to individuals according to their age, gender and level of physical activity (King, 2007). Computer technology is thus one means of adapting nutrition education programs to individuals on a large scale. As the use of such technologies becomes more widespread and we learn more about how to apply them for the better good, educational messages can be more effectively disseminated and diffused.

Finally, the demographic transition is occurring worldwide. In fact, most older adults live in developing countries. The Global Strategy on Diet, Physical Activity and Health prepared by the World Health Organization (WHO) and presented at the Fifty-seventh World Health Assembly, stresses the importance of developing and applying evidence-based nutrition and physical activity programs to maintain the health and functional capacity of the increasing elderly population and reduce the demand for, and cost of, health services (WHO, 2007). WHO issued a resolution that emphasized its involvement, in cooperation with other organizations of the United Nations system, to provide the leadership, evidence-based recommendations and advocacy for international action to improve dietary practices and increase physical activity. Improving the public health status of older adults is important for our collective quality of life and individual health care needs.

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26

Quality of feeding assistance care in nursing homes

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The most reliable way to monitor nursing home care – feeding assistance as well as all other types of care – is to directly observe how the care is provided.

Weight Loss Prevention Module, UCLA Borun Center web site (http://borun.medsch.ucla.edu)

Abstract: Nutrition is an important component of quality of life for the elderly. International studies suggest that many elderly individuals have insufficient intake of foods and fluids. For elderly individuals residing in institutions, such as long-term care (LTC) facilities, cognitive and physical impairments are two major factors that contribute to a need for staff assistance with eating. The purpose of this chapter is to review research related to the quality of feeding assistance care in the LTC setting and the implications of this care for staffing needs.

Key words: elderly, nutrition, long-term care.

26.1 Introduction

Nutrition is an important component of quality of life for both community-dwelling and institutionalized elderly. International studies suggest that many elderly individuals have insufficient intake of foods and fluids, as determined by recommended dietary allowances or other criterion (Ackner and Flöistrup, 2003; Deijen *et al.*, 2003; Simmons and Reuben, 2000; Souminen *et al.*, 2004; Wendland *et al.*, 2003). For elderly individuals residing in institutions, such as long-term care (LTC) facilities, cognitive and physical impairments are two

major factors that contribute to a need for staff assistance with eating. The purpose of this chapter is to review research related to the quality of feeding assistance care in the LTC setting and the implications of this care for staffing needs. Specifically, we will review:

- observational studies related to staff provision of feeding assistance care and delivery of oral liquid nutritional supplements;
- efficacy of feeding programs as interventions to improve LTC residents' oral intake and weight loss outcomes;
- staffing needs to implement efficacious feeding programs;
- an observational tool to monitor and improve feeding assistance care;
- a model for translating research findings into daily LTC practice; and,
- the recent movement toward culture change in LTC and its implications for mealtime care.

26.1.1 Observational studies

Many LTC residents have inadequate food and fluid intake, which places them at risk for weight loss, hospitalization, and death (Blaum *et al.*, 1995; Ferguson *et al.*, 1993). The results of recent direct observational studies suggest that residents in need of help often do not receive the assistance necessary to promote adequate food and fluid intake (Kayser-Jones and Schell, 1997; Simmons *et al.*, 2001; 2002). In these studies, research staff directly observed LTC staff delivery of foods, fluids, and assistance to residents during regularly scheduled meals (breakfast, lunch, dinner) (Kayser-Jones and Schell, 1997; Simmons *et al.*, 2001; 2002). Results showed that LTC staff members spent an average of less than ten minutes (per resident) providing help to eat during meals. When help was provided, it consisted mostly of physical assistance with little to no verbal cueing or social stimulation to enhance a resident's independence in eating and quality of life during meals (Kayser-Jones and Schell, 1997; Simmons *et al.*, 2001; 2002). Similarly, another study showed that residents were offered additional foods or fluids between meals only once per day or less, on average, again with little to no assistance or encouragement to promote consumption (Simmons and Schnelle, 2004). The results of these direct observational studies strongly suggest that the adequacy and quality of feeding assistance care provision contributes to low oral food and fluid intake in LTC residents.

A common treatment approach for poor oral intake among LTC residents is to order an oral liquid nutritional supplement (e.g., high protein nourishment, Ensure, Resource); however, studies that evaluated the effectiveness of supplements in promoting weight gain have shown mixed results (Fiaterone et al., 1994; Lauque et al., 2000). Two recent observational studies showed that, in practice, LTC staff members do not deliver supplements consistent with residents' orders nor do they provide adequate assistance or encouragement to promote consumption (Kayser-Jones et al., 1998; Simmons and Patel, 2006). The results of one study showed that LTC workers often provided supplements

to residents during regularly scheduled meals instead of between meals. These same residents received less than ten minutes of staff assistance to promote consumption of the served meal. This finding suggests that supplements may be provided in lieu of staff assistance to eat the served meal (Simmons and Patel, 2006).

26.1.2 Efficacy of feeding programs

Several anecdotal or uncontrolled studies have suggested that an increase in staff attention, social stimulation, and encouragement results in improvements in residents' oral intake (Lange-Alberts and Shott, 1994; Musson *et al.*, 1990; Van Ort and Phillips, 1995). Only recently have there been controlled intervention studies specifically designed to evaluate the effects of individualized feeding assistance on LTC residents' oral food and fluid intake during and between meals (Simmons *et al.*, 2001; Simmons and Schnelle, 2004). The individualized feeding assistance protocols evaluated in these studies included an increase in staff attention and the provision of social stimulation, encouragement, and other types of assistance with eating to promote oral intake and enhance the resident's independence in eating. Results showed that 90% of residents who consistently ate less than 75% of the served meals under usual LTC conditions significantly improved intake in response to a feeding assistance protocol implemented either during or between meals by research staff. Moreover, a two-day trial of feeding assistance was valid in determining which protocol (during versus between meals) was most effective in increasing oral intake for an individual resident (Simmons *et al.*, 2001; Simmons and Schnelle, 2004).

However, these individualized interventions implemented by research staff required significantly more time than LTC staff were directly observed to spend on feeding assistance under usual conditions. Research staff spent an average of 35 minutes per resident/meal providing assistance compared to less than ten minutes per resident/meal under usual care. The efficacious delivery of snacks between meals by research staff required an average of 12 minutes per resident/snack. In comparison, LTC staff spent less than one minute offering residents additional foods and fluids between meals. Research staff demonstrated that these efficacious feeding assistance interventions could be made more time efficient both during and between meals by grouping residents in need of assistance together in a common area (Simmons *et al.*, 2001; Simmons and Schnelle, 2004).

It is clear from these intervention studies that feeding assistance represents a key daily care process in ensuring adequate food and fluid consumption for LTC residents (Simmons *et al.*, 2001; Simmons and Schnelle, 2004). Feeding assistance also has been recognized as a key daily care process in best practice guidelines for nutritional care and evidence-based guidelines for nursing care (Ackley *et al.*, 2008; Reuben, 1999; Thomas *et al.*, 2000). Equally important, family members of LTC residents rated improvements in feeding assistance care quality as significantly more preferable than other nutritional interventions,

including the use of oral liquid nutritional supplements or medications to stimulate appetite, for their LTC relatives with poor oral intake (Simmons *et al.*, 2003b). Unfortunately, it is also clear from these intervention studies that the delivery of efficacious feeding assistance requires a significant amount of staff time (Simmons *et al.*, 2001; Simmons and Schnelle, 2004).

26.1.3 Staffing needs

Recent research strongly suggests that many LTC facilities may not have adequate staffing to provide efficacious feeding assistance care to all residents in need (Kayser-Jones and Schell, 1997; Simmons *et al.*, 2001; Simmons and Schnelle, 2004; Reuben, 1999; Schnelle *et al.*, 2000; 2004). Increases in nurse aide staffing have been recommended by multiple groups (Schnelle *et al.*, 2000; 2004; Mondoux, 1998). The recommendations focus on nurse aide staffing because nurse aides are typically the direct care providers in the LTC setting responsible for feeding assistance care provision, as well as other activities of daily living (e.g., toileting, dressing/grooming, walking assistance). An expert consensus panel recommended a ratio of one nurse aide to two physically-dependent residents or three/four semi-dependent residents during mealtimes (Mondoux, 1998). A separate study used computerized simulation technology to project nurse aide staffing levels for five different aspects of daily care, including feeding assistance. Computerized simulation technology is based on the time per episode of care and the estimated number of residents in need of care in consideration of waiting times (e.g., tray delivery) and other unexpected events (e.g., clean up and replacement of spilled foods and fluids). Results showed that a ratio of five to seven residents per nurse aide is needed on both the day (7am to 3pm) and evening (3pm to 11pm) shifts to consistently provide all five aspects of care to all residents in need (Schnelle *et al.*, 2000). A validation study in 34 LTC facilities supported the staffing recommendations from the expert consensus panel and computerized simulation studies. Findings showed that facilities with total staffing (nurse aides plus licensed nurses) above 4.1 hours per resident day performed significantly better on multiple care processes, including feeding assistance, compared to facilities with staffing below this level (Schnelle *et al.*, 2000).

LTC staff may erroneously base their staffing needs on only those residents who require extensive or total staff assistance with eating. A study with 91 LTC residents showed that the staff time to provide feeding assistance that improved food and fluid consumption was comparable across different levels of eating dependency. Across all levels, residents required an average of 35 to 40 minutes of staff time per meal; thus, residents who needed only supervision and verbal cueing required just as much staff time as those who were physically dependent on staff for eating (Simmons and Schnelle, 2006a).

In the absence of high staffing levels, it is likely that some mealtime tasks will need to be assigned to non-nursing staff. Related to this issue, a recent controversial US federal regulation was passed that allows facilities to hire ‘paid

feeding assistants', who are single-task workers and/or existing non-nursing staff trained to provide this care. Opponents of the regulation argue that a single-task work force of 'feeding assistants', who require less formal training than nurse aides, will not mitigate the need for additional staff to provide multiple other daily care processes (e.g., incontinence care, exercise, repositioning). Advocates argue that the problem of inadequate feeding assistance is so severe that LTC facilities need an immediate and inexpensive way to increase the number of available staff during meals without having the costly burden of doubling their work force. A recent preliminary study evaluated the impact of the regulation on feeding assistance care quality in a convenience sample of seven facilities in three states with active programs (Simmons *et al.*, 2007). Results showed that most (84%) of the staff trained as 'feeding assistants' in the seven facilities were non-nursing staff within the facility, and the quality of feeding assistance care provided by these workers was comparable to that provided by indigenous nurse aides. There were no reported changes in existing staffing levels (nurse aides or licensed nurses) following program implementation, and the majority of indigenous staff at all levels (>90%) reported positive benefits of the program to both staff and residents. Findings from this preliminary study indicate that the new US federal regulation may serve to increase the utilization of existing non-nursing staff to improve feeding assistance care during meals without having a negative impact on existing nurse aide and licensed nurse staffing levels (Simmons *et al.*, 2007).

26.1.4 Observational tool

There are other barriers, beyond limitations in staffing resources, to ensuring the provision of adequate feeding assistance in daily LTC care practice. For instance, LTC staff members' medical record documentation of their own provision of feeding assistance to individual residents and their estimates of residents' daily oral intake are often erroneous or completely absent (Simmons and Reuben, 2000; Simmons *et al.*, 2002; 2003a; Schnelle *et al.*, 2004; Kayser-Jones *et al.*, 1997; Pokrywka *et al.*, 1997). In both cases, medical record documentation reflects a significant overestimate compared to independent observational measures by research staff (Simmons and Reuben, 2000; Simmons *et al.*, 2002; 2003a; Schnelle *et al.*, 2004; Kayser-Jones *et al.*, 1997; Pokrywka *et al.*, 1997). The error in nurse aide estimation of residents' daily oral intake prevents licensed nurses from accurately identifying residents at risk for under-nutrition, dehydration, and unintentional weight loss due to low intake. The inaccuracy of medical record documentation related to feeding assistance impedes the ability of supervisory-level staff (licensed nurses) to effectively manage the consistency and quality of daily care delivery. Finally, there are aspects of feeding assistance provision not documented by LTC staff but important to monitor to ensure care quality and residents' associated quality of life. For example, in the US, the LTC staff is not required to document type of feeding assistance (e.g., verbal cueing versus physical assistance), amount of

time spent providing feeding assistance, or resident consumption of foods and fluids, including oral liquid nutritional supplements, provided between regularly scheduled meals.

26.2 Quality assessment

26.2.1 An observational tool

The inaccuracies and missing data in medical records create a need for information independent from the medical record that can be used to monitor daily feeding assistance care delivery and quality. A time-efficient, informative, direct-observational tool has been developed and used in multiple LTC facilities that allows supervisors to collect accurate information necessary to effectively manage daily feeding assistance care delivery and monitor the accuracy of related medical record documentation (see Table 26.1) (Simmons *et al.*, 2002; 2003a; Schnelle *et al.*, 2004). The information generated by the observational tool can be reported as feeding assistance quality indicators (e.g., proportion of residents within a facility who had low oral intake but who did not receive assistance from LTC staff during a particular meal).

There are two primary advantages of a quality indicator (QI) score. First, a QI score has the potential to highlight clinically significant care quality problems (i.e., care areas in need of improvement). Second, a QI score efficiently summarizes the data into understandable quality categories for which feeding assistance can be scored as either 'passing' or 'failing' for individual residents and mealtime periods. The percentage of residents who receive a 'pass' or 'fail' score provides a summary measure of the quality of care provision, which is useful for making comparisons within a facility over time (e.g., staff shifts, meals).

The rules and rationale that guide the scoring of eight feeding assistance care QIs are presented below. These eight QIs, which are based on previous work (Simmons *et al.*, 2002; 2003; Schnelle *et al.*, 2004), are operationalized into specific LTC staff behaviors that can be reliably observed during meals. The focus on care processes under the direct control of LTC staff is critical to any quality improvement effort, because it is possible for poor clinical outcomes to occur (e.g., unintentional weight loss) in the context of optimal care quality. The scoring rule for each QI reflects a liberal approach that maximizes the opportunity for staff to 'pass'.

26.2.2 Feeding assistance care quality indicators for meals

Staff ability to get residents out of bed and to the dining room for meals

Scoring rule: Score as 'fail' if less than half of the resident population, as defined by those residents capable of oral food and fluid intake (exclude residents who are bed-bound, tube-fed and/or on hospice), is eating the meal in the dining room or other common location. Count all dining rooms and other common eating area(s).

Rationale: Residents eating in the dining room are more likely to receive help to eat from staff, social interaction during the meal, and accurate documentation of their food and fluid intake (Simmons and Levy-Storms, 2006a). Residents often eat meals in their rooms in bed not necessarily because they want to, but because it is easier for staff (Simmons and Levy-Storms, 2006b). Moreover, residents who eat in their beds are often improperly positioned for eating (semi-reclined), which places them at greater risk for choking. Finally, social isolation during meals may contribute to low oral intake and depressive symptoms.

Staff ability to provide a verbal prompt to residents who receive physical assistance with meals

Scoring rule: Score as 'fail' any resident who receives physical assistance from LTC staff during the meal without also receiving at least one verbal prompt directed toward eating (e.g., 'Please try your beans.') at any point during the meal.

Rationale: Graduated prompting protocols that use verbal prompts have been shown to increase residents' independent eating behaviors and oral food and fluid intake (Simmons *et al.*, 2001; Simmons and Schnelle, 2004; Lange-Alberts and Shott, 1994; Van Ort and Phillips, 1999). Multiple groups have suggested that verbal prompting coupled with physical assistance defines optimal feeding assistance care (Ackley *et al.*, 2008; Reuben, 1999; Thomas *et al.*, 2000). Observational data indicate that LTC workers often provide excessive physical assistance to residents who could otherwise eat independently with just verbal prompting or encouragement (Simmons *et al.*, 2001; Simmons and Schnelle, 2004). Ideally, the verbal prompt should precede physical assistance to encourage independence in eating; but, the scoring rule for this indicator allows LTC staff to 'pass' if a verbal prompt is provided at any point during the meal (before, during, or after physical assistance).

Staff ability to provide social interaction to all residents during mealtimes

Scoring rule: Score as 'fail' any resident who does not receive at least one episode of social interaction (i.e., verbal interaction that does *not* include a specific instruction to eat; e.g., 'How are you today?', or 'It's nice to see you in the dining room') at any point during the meal.

Rationale: Social interaction has been shown to increase oral food and fluid intake in LTC residents. Social interaction during meals is also important to residents' quality of life and, thus, should not be limited to those with low oral intake (Simmons *et al.*, 2001; Simmons and Schnelle, 2004).

Staff ability to provide adequate feeding assistance to residents who receive an oral liquid nutritional supplement with meals

Scoring rule: Score as 'fail' any resident who receives an oral liquid nutritional supplement and less than five minutes of staff assistance to eat during the meal.

Table 26.1 Mealtime observational tool

Date: ____ / ____ / _____ Staff Observer: _____ Begin Time: ____:____ am pm

End Time: ____:____ am pm

Meal: ___Breakfast ___Lunch ___Dinner Location: ___ Dining Room ___ Room/Hall

Identify 4–8 residents who should receive feeding assistance (e.g., rated on MDS as requiring assistance to eat, history of weight loss).

Observe during the meal and record all information below.

	1	2	3	4		5		6		7	8	
Resident Name	Physical Assist	Verbal Instruction	Social Stimulation	Supplement Yes	Consumed	Assist Time >5 min	<5 min	Total % Eaten >50	<50	Medical Record Total % Eaten	Assistance Provided	Comments (resident complaints about meal or staff offers of substitutions?)
					oz							
					oz							
					oz							
					oz							
					oz							
					oz							
					oz							
					oz							

Calculate feeding assistance care process measures below as a percentage (0% to 100%) for residents observed during this meal.

1. What proportion of resident population is eating in the dining room? (total number in dining room(s) / total residents capable of oral intake) _____%
2. Of those who received physical assistance (column 1), how many also received verbal instruction (column 2)? _____%
3. Of the total number of observed residents, how many received at least one episode of social stimulation from staff (column 3)? _____%
4. Of those who were given a supplement (column 4. yes), how many received more than 5 minutes of assistance (column 5. > 5)? _____%
5. Of those who ate less than 50% (column 6. <50), how many received more than 5 minutes of assistance (column 5. >5)? _____%
6. Of those who ate less than 50% (column 6. <50), how many were offered a substitution (see comments)? _____%
7. Of those who ate less than 50% (column 6. <50), how many had documentation equal to or less than 60% (column 7. total % eaten)? _____%
8. Of those who had documentation assistance was provided (column 8), how many received more than 5 minutes of assistance (column 5. > 5)? _____%

Observational definitions	Record all types of assistance provided by any type of staff during the meal (from tray delivery to tray pick up), even if it only occurs once.
Physical assistance/Physical guidance	Staff holds utensil/cup and/or helps resident to hold utensil/cup to eat or drink (e.g., aide feeds resident or physically assists resident to feed him or herself).
Verbal instruction (cueing, reminders)	A comment made by staff specifically directed toward eating (e.g., 'pick up your spoon and take a bite'; 'try some more of your soup').
Social stimulation	A social comment made by staff NOT specifically directed toward eating (e.g., 'How are you today? It's good to see you. You look nice today').
Supplement	Record any type of oral liquid nutritional supplement (e.g., Resource, High Protein Nourishment, Ensure) given with the meal and amount consumed by resident.
Assistance	Record estimated time spent by any type of staff (nurse aide, licensed nurse, feeding assistant) providing any type of assistance to encourage eating during the meal.
Total percent eaten	Calculate on a 0% to 100% metric using the same measurement system required of nurse aides, or other designated staff, in the facility.
Medical record	Documentation of total percent eaten and assistance provided by nurse aide or other staff for the same day and meal as observation.
Comments	Record resident complaints about meal service or appetite, staff offerings of substitutions for served meal or other relevant observations (e.g., refusal of food or help).

Rationale: Oral liquid nutritional supplements are most effective in increasing daily caloric intake among LTC residents when provided between regularly scheduled meals as opposed to with meals. Direct observational data suggest that supplements are often inappropriately given with meals and may be used as a substitute for quality feeding assistance (Kayser-Jones *et al.*, 1998; Simmons and Patel, 2006). Thus, residents should not be given a supplement during the meal unless staff have provided assistance to encourage the resident to eat the served meal.

Staff ability to provide assistance to at-risk residents

Scoring rule: Score as 'fail' any resident who consumes less than 50% of the food and fluid items on his or her meal tray based on direct observation and who receives less than five minutes of feeding assistance from LTC staff during the meal.

Rationale: Residents who consume less than 50% of the served meal are at greater risk for weight loss (Gilmore *et al.*, 1995). If a resident who consumes less than 50% of a meal also receives less than five minutes of feeding assistance from LTC staff, then the staff is providing potentially substandard feeding assistance, failing to recognize an oral intake problem, or both. The five-minute criterion allows for the delivery and removal of the meal tray even if no assistance to eat is provided to the resident (Reuben, 1999; Simmons *et al.*, 2003a).

Staff ability to offer meal alternatives to residents who do not like the served meal

Scoring rule: Score as 'fail' any resident who eats less than 50% of the food and fluid items on his or her meal tray based on direct observation, and who is not offered a meal alternative (i.e., substitution) at any point during the meal by any staff member.

Rationale: Residents often do not like the served meal or certain items on the meal tray; however, most residents will not complain directly to staff about the meal service or request other foods. Thus, it is important for staff to notice when a resident is not eating well and offer him or her alternatives to the served meal or individual foods or fluids (e.g., a different kind of sandwich or fruit, orange juice instead of apple juice, sausage instead of bacon) (Reuben, 1999; Simmons *et al.*, 2003).

Staff ability to accurately identify residents with clinically significant low oral food and fluid intake during meals

Scoring rule: Score as 'fail' any resident who consumes less than 50% of the food and fluid items on his or her meal tray based on direct observation, but who is identified by the LTC staff (i.e., medical record documentation of percentage intake for the same meal as the observation) as consuming equal to or greater than 60%.

Rationale: The US federal criterion for low oral intake among LTC residents is defined as 'leaves 25% or more of food uneaten', or consumes less than 75%

of most meals (Minimum Data Set, 1999). Recent evidence, however, suggests that LTC residents who consistently consume less than 50% of most meals are at a significantly higher risk for weight loss (Gilmore *et al.*, 1995). Thus, if the staff documents that a resident consumed more than 60% of a meal when, in fact, the resident ate less than 50%, it is likely that the staff are failing to identify a clinically significant oral intake problem for that resident (Simmons *et al.*, 2002; 2003a).

Staff ability to accurately document feeding assistance care provision

Scoring rule: Score as 'fail' any resident who receives less than five minutes of assistance from staff but who has medical record documentation for the same day and meal that feeding assistance was provided.

Rationale: Studies have shown that feeding assistance is documented in the medical record as provided for all residents at risk for weight loss (those rated by the LTC staff as requiring assistance to eat and/or those with a history of weight loss), even though most of these residents actually receive less than five minutes of assistance (Simmons *et al.*, 2002; 2003). Thus, medical record documentation related to feeding assistance care provision is not accurate or specific enough to be useful for quality assessment or improvement efforts.

26.2.3 Use of quality indicators for feeding assistance care

These eight QIs are examples of the type of information that can be gathered by supervisory-level staff using the direct observational tool presented in Table 26.1. Additional QIs for care processes related to weight loss that can be measured through direct observation, medical record abstraction, and/or resident interview using standardized protocols have been described elsewhere (Reuben, 1999; Simmons *et al.*, 2003). Regardless of which QIs are used, the observational tool should be feasible to implement by supervisory-level LTC staff members. Based on our previous work, we estimate that supervisors should conduct observations during one to three meals (breakfast, lunch, and dinner) per week to effectively monitor the adequacy and quality of daily feeding assistance care provision. The tool focuses on specific care processes that can be measured and controlled by the LTC staff, which makes it useful for quality assessment and improvement purposes. The tool is not intended to comprehensively assess all issues relevant to nutritional care in the LTC setting; rather, it is a tool that supervisory-level LTC staff members can use to monitor the quality of feeding assistance provided to residents as well as the accuracy of corresponding medical record documentation.

26.3 Translation of nutrition interventions into practice

The development of efficacious behavioral interventions to improve LTC residents' daily food and fluid consumption represents an important advance in

research (Simmons *et al.*, 2001; Simmons and Schnelle, 2004). A critical next step is to translate these efficacious interventions into LTC practice. The UCLA Borun Center has developed standardized assessment protocols and instructions accessible via the web (http://borun.medsch.ucla.edu) by LTC providers to support the translation of these interventions into care practice. Our research team has pilot tested this translational research model through the support of the UCLA Pepper Center and a Quality Improvement Award from the American Medical Directors' Association and Pfizer. Briefly, we conducted a pilot quality improvement study in one skilled LTC facility wherein we trained the nursing staff to implement the individualized feeding assistance protocols (nurse aides) and monitor care quality via the direct observational tool (supervisory-level staff). There were significant improvements in feeding assistance care processes, as measured by the QIs, following four months of implementation (Simmons and Schnelle, 2006b).

The advantage of the observational tool for quality assessment and improvement efforts is that the tool focuses on care processes under the direct control of LTC staff (e.g., feeding assistance) as opposed to clinical outcomes (e.g., weight loss). In addition, the protocol is standardized and time-efficient, which allows multiple independent observers to produce consistent conclusions about quality within the constraints of the LTC quality assurance and survey process. One important area of new research is to improve the consistency of the US federal survey process in detecting nutritional care quality problems. We believe the use of standardized observational tools is feasible during the survey process and would greatly increase the motivation of LTC care providers to conduct similar observations for quality assurance purposes on an ongoing basis. Our research team is currently conducting a study sponsored by the federal Centers for Medicare and Medicaid Services that will incorporate standardized observational tools to evaluate nutritional care quality, such as that presented in Table 26.1, into the survey process.

Lastly, an issue to consider in improving LTC staff delivery of foods and fluids between meals is the dietary service cost. However, it may be possible to offset the cost if palatable food and fluid items are consistently offered to residents between meals instead of oral liquid nutritional supplements. Previous research suggests that both family members and residents prefer a variety of snack items from which to choose over supplements (Simmons and Schnelle, 2004; Simmons *et al.*, 2003b). The cost-effectiveness of using snacks compared to oral liquid nutritional supplements to prevent weight loss among LTC residents is currently being evaluated by our research team through support from the National Alzheimer's Association.

26.4 Culture change at mealtimes

Mealtimes in LTC facilities demonstrate a strong relationship between LTC residents' quality of life and the quality of care they receive. The staff feeding

assistance behaviors advocated in this chapter, for example, stem from an effort to improve quality of care, but address as well what are commonly viewed as quality-of-life concerns. Hence, we recommend that staff socially interact with residents to enhance the mealtime ambience, and with it, increase residents' food and fluid intake. We also advocate serving residents food that they like. Conversely, dining room routines are undergoing transformation in some LTC facilities as part of a concerted effort to improve quality of life by delivering resident-directed care; however, as we discuss in this section and the next, these changes may fall short of their expected outcomes unless they also address what are commonly viewed as quality-of-care concerns.

These mealtime reforms are advocated by proponents of the LTC culture change movement, a rapidly expanding grassroots effort aimed at creating real homes within nursing homes and engaging empowered residents and direct care staff in 'households' where both can flourish. Since winning support in the US from the Centers for Medicare and Medicaid Services in 2005, when this federal agency directed state Quality Improvement Organizations to work with facilities to 'improve organizational culture,' the movement has become an increasingly powerful force for effecting change in LTC facilities. And mealtimes, rife with often unrealized potential to bring pleasure to residents, are a frequent focus of culture change reformers around the globe.

'Mealtimes (in LTC facilities) are usually the main social events of the day,' write Greene Burger *et al.* (2000). 'When well planned, they can invoke strong memories of home, family, and friends' (p. 34). Regrettably, in most facilities they invoke something quite different. Writing about the inner world of LTC facilities for a review in *The Gerontologist*, Olsen (2006) describes an unsavory dining room scene: 'Food tends to be uninviting, tasteless, without texture, watery, overcooked, and occasionally inedible. Hot meals and coffee often are served cold. There are only limited, if any, menu choices . . . residents are herded and shoved to meals by overwhelmed aides.' And that's not all. According to Greene Burger *et al.* (2000, p. 34): 'Those (residents) who are taken to, or can walk to, the dining room must usually eat in chaotic settings – with televisions blaring, staff members calling to one another over the residents' heads, and residents dressed inappropriately – that do not facilitate socialization or encourage the intake of sufficient food.'

Clearly there is room for improvement, and recognizing this, more and more LTC facilities are experimenting with culture changes designed to enhance the residents' dining experience. These changes generally fall under three broad categories:

- Aesthetic changes: The impetus for these changes stems from the notion that a meal's presentation can enhance or diminish the diner's enjoyment of the meal itself. Aesthetic changes include using fine china and glassware, decorating tables with attractive tablecloths and centerpieces, seating residents in chairs rather than wheelchairs, and playing soft background music. Also included is the elimination of items commonly associated with meals in institutions, such as trays and small milk cartons.

- Changes in service hours: Rather than serving meals at designated hours (e.g., 8 a.m., noon, and 6 p.m.), culture changing facilities offer flexible mealtimes so that residents have greater choice. Some facilities serve meals over an extended period. Breakfast, for example, might be served anytime between 8 a.m. and 10 a.m. Another option is the open breakfast, which allows residents to enjoy their first meal of the day whenever they want. Some LTC facilities are sectioning their interiors into small households and neighborhoods, each with their own small kitchen. In these facilities, residents may have greater access – almost 24/7 – to between-meal snacks.
- Changes in meal service: Culture changing facilities are experimenting with cozier, homier alternatives to serving pre-plated meals to residents in large dining rooms. One goal of these innovations is to offer residents more choice in selecting food items. Some facilities, for example, are serving meals buffet style while others are dishing it up family style, with bowls and platters of food placed centrally on each table. Other alternatives include serving resident-selected meals from steam tables and food carts that can be rolled from one room to another or from one 'household' to another.

All of these changes seem reasonable and are intuitively appealing. Moreover, there is some evidence to suggest that LTC residents welcome them (Walton *et al.*, 2006). Yet LTC facilities interested in implementing any of these culture change interventions should proceed with caution for two reasons. First, few of these mealtime culture changes have been evaluated, and the studies that have been conducted are of mixed quality and have shown mixed results (Remsburg *et al.*, 2001; Gibbons and Henry, 2005; Hotaling, 1990; Marie-Francoise *et al.*, 2001; Nijs *et al.*, 2006a; 2006b). Perhaps the strongest and most promising results to date have been reported for family-style meals and non-institutional aesthetic changes, which were evaluated in three recent studies. In one study, Dutch researchers found that LTC residents ate more when meals were served family style (Nijs *et al.*, 2006a). In a second paper, the researchers reported that this same meal-service intervention prevented a decline in quality of life, physical performance, and body weight among LTC residents without dementia (Nijs *et al.*, 2006b). However, the intervention, as noted in both papers, instructed nursing staff to converse with residents during the meal. Thus, a noteworthy caveat applies: 'The social interaction during these meals increased by the extra attention residents received from the nurses who were sitting at the tables,' the authors observe (Nijs *et al.*, 2006a). 'In this study, we cannot say which part of the intervention protocol had the most impact on the residents. The protocol we used has to be considered as one package.'

In the third study, an observational study of mealtime routines in 45 LTC and assisted living facilities, the presence of non-institutional features such as tablecloths were associated with increased food and fluid intake among a sample of 407 residents with dementia (Reed *et al.*, 2005).

These results are promising, but preliminary; despite them, we still know

relatively little about the effectiveness of the myriad mealtime culture changes underway in LTC facilities.

The second reason for acting cautiously is that, while these culture changes seem desirable, they do not go far enough. Ironically – for a movement centered on giving a voice to residents and empowering line staff – culture change proponents have been silent about the need to improve resident-staff interactions during meals, despite the fact that the majority of LTC residents require some staff assistance to eat – ranging from verbal reminders to physical assistance – and problems with staff delivery of feeding assistance have been widely reported. An observation by a LTC ombudsman describes a disturbing but regrettably not uncommon mealtime scenario:

> I watched a man trying to feed himself breakfast. He had spilled his milk and coffee. The toast was on the floor. He was trying to eat cold cereal and milk with a spoon but most of it never reached his mouth. After about 15 or 22 minutes he just gave up. There was an aide sitting in the day room with him. She was reading the paper and never even looked up (Greene Burger *et al.*, 2000, p. 21).

One might hope, but would be foolish to assume, that long-practiced staff behaviors would change as a result of serving meals family style or on fine china on a decorated table. To truly enhance residents' dining experience and, with it, quality of life, culture changes need to go beyond improving aesthetics and expanding service options. Also needed is staff education that promotes behaviors associated with optimal feeding assistance (see the QIs presented earlier in this chapter). Additionally, supervisors should regularly monitor mealtimes to reinforce these staff behaviors.

26.5 Future trends

With limited research currently available, important questions about mealtime culture changes remain:

- How do the changes, singly or in some combination, affect clinical outcomes such as weight loss or gain?
- Do they in fact increase resident, family and/or staff satisfaction with mealtimes?
- Are they feasible to implement, especially given that many LTC facilities are understaffed at mealtimes?
- What are the advantages and disadvantages, in terms of material costs, staffing requirements, and resident preferences, of one change (or a combination of changes) relative to another?

As these questions suggest, more research is needed to determine best practices in LTC dining rooms. For now, however, LTC facilities, few of which can afford to waste staff time and resources on dead-end interventions, would do

well to explore these questions with their staff and residents before proceeding with costly or time-consuming mealtime innovations. Once a new intervention is initiated, facilities should monitor the care process using the direct observational tool available in Table 26.1 to ensure that the quality of feeding assistance is not compromised as an unintended consequence.

26.6 Conclusions

Mealtimes have always offered an opportunity to nourish both the body and the soul. It seems especially important to take full advantage of this opportunity in LTC facilities, where so many frail residents are vulnerable to conditions that adversely affect the mind, body, and spirit. To meet the complex needs of this population and provide residents with a satisfying mealtime experience, LTC facilities need to address both quality of care and quality of life concerns. One strategy for doing so is to enhance the provision of feeding assistance to LTC residents. This chapter discussed eight QIs that are operationalized into specific staff behaviors that together define optimal feeding assistance. Routinely practicing these staff behaviors helps ensure that LTC residents, especially those at risk for unintentional weight loss, receive the physical and social support needed to maximize their food and fluid intake. Additionally, LTC supervisors can readily monitor these staff behaviors using a direct observational tool we developed for this purpose. This ready-to-use tool can help maintain quality of care, a distinct advantage in those countries that report quality assurance as a weak spot in their LTC systems (AARP, 2003).

Efforts are underway to facilitate the translation of these efficacious protocols into LTC practice. Recognizing that enhanced feeding assistance takes more time to provide than usual care, special attention is being directed to ensuring that the protocols are feasible for staff to implement. This focus is especially important given that many countries report LTC labor shortages (AARP, 2003). Creative and targeted use of both nursing and non-nursing staff will likely be needed to deliver high quality feeding assistance to all LTC residents who need it.

Also underway are efforts to transform dining routines as part of a concerted effort to improve the culture of LTC and enhance quality of life by delivering resident-directed care. LTC facilities in all parts of the world are striving to deliver more home-like meals to their residents by experimenting with aesthetic changes in the dining room as well as innovations in service styles and meal times. While these changes seem reasonable and are intuitively appealing, they are largely untested. More research is needed to answer questions about their efficacy, feasibility, and relative advantages and disadvantages. In the meantime, we recommend that culture changing LTC facilities use our mealtime QIs and the observational tool presented in Table 26.1 to monitor their staff's quality of feeding assistance as new interventions are introduced. LTC residents seem likely to benefit most when interventions focus dually on quality of care and quality of life.

26.7 Sources of further information and advice

The Centers for Medicare and Medicaid Services recently (March 16, 2007) launched a web-cast titled 'How to Enhance the Quality of Dining Assistance in Nursing Homes' wherein feeding assistance techniques, as defined by the QIs and the observational tool discussed in this chapter, are reviewed for LTC providers (http://www.cms.internetstreaming.com). The web-cast is applicable to both direct care (nurse aide) and supervisory-level (licensed nurse) staff.

Detailed instructions and protocols for implementing the efficacious feeding assistance interventions described in this chapter are available online from the web site of the University of California Los Angeles Borun Center for Gerontological Research at http://borun.medsch.ucla.edu. The 'prevention of weight loss' training module, available at no cost as a service to the long-term-care community, is organized around four steps:

1. Assess resident risk for weight loss.
2. Individualize feeding assistance.
3. Implement new staffing strategies.
4. Monitor quality of feeding assistance.

All the forms needed to implement the intervention can be downloaded from the web site. Also included are a pre- and post-training quiz, frequently asked questions with answers, background research on the topic, and links to related web sites. Nurses can earn two contact hours – also offered at no cost – for completion of the module.

In addition to the weight loss prevention module, the Borun Center web site offers online training modules designed to help LTC staff improve care in five related care areas:

- incontinence management
- pain screening
- pressure ulcer prevention
- mobility decline prevention
- quality-of-life assessment.

The entire training series works together to provide a holistic approach to improving daily care and enhancing quality of life for LTC residents. All of the modules are based on a series of intervention studies that have won wide acclaim for producing cost-efficient and effective methods for improving LTC. The following web sites also offer online resources for improving nutritional care among the elderly and LTC residents:

- American Association of Diabetes Educators
  http://www.aadenet.org/
- American Diabetes Association
  http://www.diabetes.org/home.jsp
- American Dietetic Association
  http://www.eatright.org/Public/index.cfm

- American Medical Directors Association
  Clinical Practice Guideline: Altered Nutritional Status
  http://www.amda.com/tools/cpg/nutritionalstatus.cfm
- American Society for Nutrition
  http://www.nutrition.org/
- Dietary Managers Association
  http://www.dmaonline.org/
- International Academy of Nutrition and Aging
  http://www.healthandage.com/html/min/iananda/index.htm
- Medicare
  Nursing Home Awareness Campaigns
  Nutrition and Hydration Awareness: Nutrition Care Alert
  http://medicare.gov/Nursing/Campaigns/NutriCareAlerts.asp
- LTC Regulations Plus
  http://www.hpm.umn.edu/LTCRegsPlus/index.htm
  Lists federal regulations for nursing home dietary services

26.8 Acknowledgements

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27

Preparing meals in later life

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Abstract: This chapter deals with food used to prepare meals in the private households of older people. At first, attention is given to the different types of food available and used to prepare meals at home, focusing on meal preparation and the use of convenience foods in later life. Successively, attention is paid to the factors that determine and influence meal preparation and food choice, or changes and problems with regard to meal preparation in old age. Finally, empirical findings from the European project *Food in Later Life,* concerning foods which ease meal preparation, are summarized.

Key words: older people, meal preparation, convenience foods, attitudes, food choices.

27.1 Introduction

The aging process, with its physiological and social consequences, can alter an individual's approach to food, thus restricting access to adequate amounts and types of food and limiting variety and a satisfactory nutrient intake. Several studies have identified factors that encourage or discourage the inclusion of specific food items and barriers to effective decision making about older people's diets (McKie, 1999; Souter and Collen, 2002; Mioche *et al.*, 2004). Physiological and psychological decline and other conditions can result in older people having related mobility problems thus finding it difficult to procure and prepare food (Rovner and Ganguli, 1998; Keller *et al.*, 1999). However, poor cooking skills (this refers to both not having the capacity and/or ability to cook) and little or no motivation to change eating habits may constitute barriers to improving energy intake, healthy eating and meal preparation (Lilley, 2002; Hughes *et al.*, 2004).

This chapter deals with food used to prepare meals in the private households of older people. On the one hand, attention is given to the different types of food available and used to prepare meals at home, with particular attention being given to those that are easy to handle. On the other hand, attention is paid to the factors that determine and influence meal preparation and food choice (Herne, 1995) such as older people's attitudes to food and food-related behaviours, or changes and problems with regard to meal preparation in old age.

Throughout the food chain there is an increasing interest in providing food items and full meals that can conveniently replace homemade meals or parts thereof. These offerings are complex and difficult to define clearly. Different terms are intended to reflect the various preservation properties and degrees of readiness for consumption, but this is not always perceptible to the consumer (Costa *et al.*, 2002). Industrially pre-prepared products will be discussed as to their relative importance in the households of independently living older people.

Products or foods that ease preparation are often given or equated (Souter and Collen, 2002) with the attribute 'convenience'. As there are many definitions of 'convenience', here convenience products are simply being seen as products 'of a higher processing level than the raw material' (according to Paulus, 1977). This follows on from the European Parliament (2002) the term 'food' in which 'food' (or 'foodstuff') means 'any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans'.

The first section gives an overview of foods available as 'initial material' for meal preparation in private households. The initial material available to the consumer dictates the range of processes they need to use to prepare a meal ready for eating. This section is followed by a short literature review concerning older people's behaviour and attitudes in respect of foods used for meal preparation. The last two sections summarize empirical findings from the European project *Food in Later Life* conducted in nine centres of eight European countries (Denmark, United Kingdom, Germany, Italy, Poland, Portugal, Spain, Sweden). This project examined changes and problems that arise during meal preparation in old age and perceptions of older consumers towards food products with convenience in preparation.

27.2 Meal preparation and the use of convenience foods in later life

27.2.1 States and convenience classes of foods (products) used for meal preparation in private households

Meal production in private households, even if only focused on choice and use of the initial material for production of meals, is determined by a multitude of different factors. The types of food chosen depends to a great extent on the available resources and production conditions such as money, kitchen equipment for production and preservation, allotment or own garden, degree of self reliance

with regard to food, time, knowledge about nutrition and cooking skills. Meal production encompasses the full range from producing from raw unprocessed material for each component of a meal to a ready-to-eat meal delivered from outside the household.

There are classifications and definitions concerning convenience foods available that are mainly developed for industrial purposes to show the different stages of industrial processed foods as replacements for meals or dishes cooked at home (BLL, 1972; Paulus, 1977; Costa *et al.*, 2001; Costa, 2003), or to distinguish between 'convenience' and 'fast' foods (Pepper, 1980). Another typology of convenience in meal preparation was drawn up by Scholderer and Grunert (2005) which combines what is being saved (time, physical and mental energy) by using different products during the different stages of consumption. But there is no general valid system or classification available which describes the conceivable mouldings of foods as the base for meal preparation and the connected net product in private households.

Efforts have been made to identify food product classification schemes which reflect a more consumer- or household-oriented perspective in which industrially prepared convenience products are only one aspect (DGH, 1968, 1975, 1979, 1984, 1992; Harrison, 1979). Definitions of terms that characterize the technical processes applied in kitchens in private households or institutional food services were extended and updated in several editions of the German Society of Home Economics' (DGH) publication (DGH, 1975, 1979, 1984, 1992). In the second edition (DGH, 1975) the classification of foods pre-processed by industry and commercial enterprises (Fig. 27.1) was shown the first time, highlighting the remaining processes to be done by the users at home. It

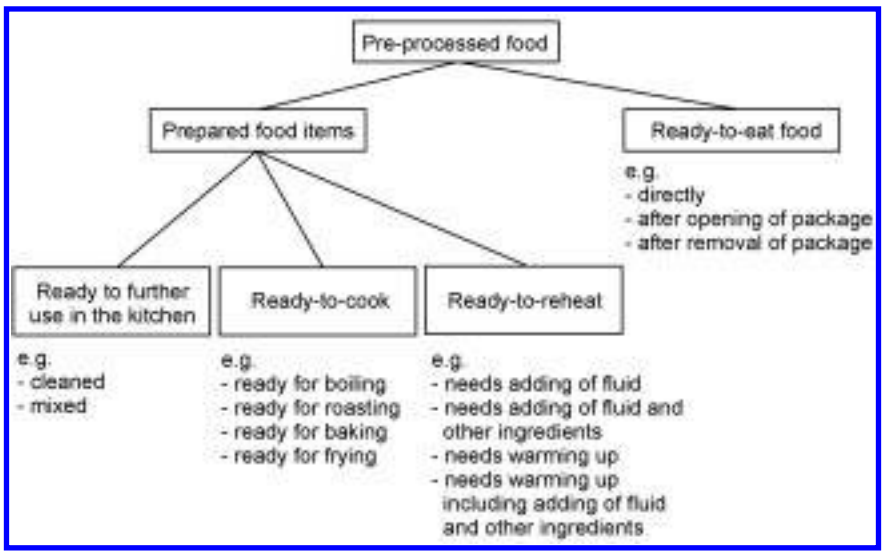

Fig. 27.1 Classification of foods that are pre-processed by industry and commercial enterprises (according DGH 1975, 1992, translated by author).

Table 27.1 Degrees of processing and states of foods used in private households, conceivable food products are designated with an 'x'

State[a] of food	Degree of processing/convenience class				
	Raw, un-processed	Ready to further use in the kitchen/ ready for kitchen processing	Ready-to-cook	Ready-to-heat/ to-reheat	Ready-to-eat
Fresh	x	x			x
Chilled	x	x	x	x	x
Deep-frozen		x	x	x	x
Pasteurized		x	x	x	x
Sterilized		x	x	x	x
Dried		x	x	x	x
Fermented		x	x	x	x
Freeze-dried				x	

[a]Combinations of states are possible, e.g. vacuum-packed & fresh, vacuum-packed & chilled
From DGH (1992)

also included an adaptation and extension of terms describing pre-processed products suitable for use in private households. All the processes applied in food preparation from scratch in private households are defined (DGH, 1992). These include preparatory methods (e.g., peeling, cutting), thermal treatments (e.g., baking, roasting), processes like warming up or regenerating, preservation methods for storage (e.g., drying, sterilizing and deep-freezing). Harrison's scale of convenience (1979) was developed for caterers, manufacturers and industry but the description and definitions of some levels of convenience are equally valid for either the meal production or the food used for preparation in private households, and are similar when compared with the definitions described above (DGH, 1975, 1992).

It is possible to characterize food available for household processing (Table 27.1) with regarding to (1) the degree of processing, i.e 'convenience' classes (e.g., raw/unprocessed, ready-to-eat) and (2) the state, i.e. kind of preservation (e.g., fresh, deep-frozen). All processing steps can be achieved in a household environment with appropriate skills and equipment, whereas it is not possible to achieve all types of special preservation methods; some processes can only be carried out in an industrial environment (e.g., freeze-drying, high pressure treatment).

The kinds of foods used for meal preparation at home depends also to a great extent on the food group or the kind of dish to be prepared. Within each food group products can span from homemade through to industrially prepared versions. Most milk and dairy products, with the exception of homemade yoghurt, etc., and products like cereals and flours, are bought, i.e. not home-made. Interestingly bread is often viewed by consumers as being only a basic food when bought. However, when bought, bread is a pre-processed product of

the highest convenience level, especially if sliced. But bread, cakes and pastries, jam, marmalade and jellies and other products for reserve like sterilized and deep-frozen vegetables and fruit are traditionally home made in many households of older people. In urban households meat of the lowest convenience level will be obtained in most cases as a product which is ready to further use in the kitchen like seasoning and roasting; the processing of half carcasses won't be the rule.

'Ease of preparation' is subjective. People who want and are used to preparing dishes from scratch and who have knowledge and skills will be critical with regard to 'ease of preparation'. These people may only use ready-to-eat products when circumstances reveal advantages that were not previously apparent, e.g. saving of time, maintaining independent meal preparation in spite of health problems that hinder cooking from scratch. For these people 'ease of preparation' starts with a slightly higher degree of convenience than the raw product, e.g. fresh cut vegetables, minced meat. It may be the case that people who are forced to provide themselves with meals without the necessary cooking experience and skills associate 'ease of preparation' with ready-to-reheat or ready-to-eat meals.

27.2.2 Convenience products and older people: perceptions and use

In the age group of 65 years and older, self preparation of meals and using fresh and (often in the case of fruit and vegetables) unprocessed ingredients is widespread in European countries (Pfau and Piekarski, 2001, Hayn *et al.*, 2005). A representative poll in Germany showed that people over 50 had the lowest rates of agreement in respect to the statement 'ready-to-eat meals make it very easy for me' (Hubert Burda Media, 2005) and had the highest agreement rates in regard to the statement 'I like cooking very much' (SevenOne Media, 2005).

Nevertheless there is an increasing use of pre-processed products in European countries (Gracia and Albisu, 2001), also by older people. Hautvast *et al.* (1992) reported a wide consumption of ready-to-eat meals among Europeans between 70 and 75 years of age. In the same European study on seniors' nutrition Schlettwein-Gsell *et al.* (1991) found that older people living in French, Swiss, and Danish towns bought convenience foods (ready-made meals for reheating) more frequently than those living in Dutch and Norwegian towns. Hayn and colleagues (2005) found that 34% of people over 60 years and 72% of people in the age between 14 years and 39 years were consumers of ready meals in Germany. Ready-made meals for reheating were widely used by older adults in towns where, at the same time, two-thirds of subjects consumed home-produced foods indicating that a multi-faceted approach to nutrition had reached the generation of elderly as well (Schlettwein-Gsell *et al.*, 1991).

In a study investigating the extent to which older consumers are set in their ways and resistant to change and innovation (Leek *et al.*, 2001), it was found that they were marginally more likely than the younger consumers to try, and willing to pay a premium price for, a new food product linked to healthy eating.

Innovations and services are adopted by the elderly if they are found appropriate to their needs and lifestyle (Leek *et al.*, 2001). However, it is important to point out that resisting innovation is not something particular to older people. Consumers in general resist innovation because they may be comfortable with their existing situation and therefore are not motivated to change (Leek *et al.*, 2001).

Older adults identified ready meals as foods that freed them of the responsibility of the preparation (Souter and Collen, 2002) and they are also associated with lower expectations and demands of a meal when family members are absent. The typical weekday dinner finds itself somewhere between the pure 'ready prepared' product and the genuine 'home-made meal' (Bugge, 2003).

Negative views of pre-processed products with high convenience levels can be found in various European countries. Sidenvall and colleagues (2000) found that older women in Sweden showed no positive attitudes towards ready-to-heat or ready-to-serve foods. Ready-to-serve food seemed to have a low cultural and moral value in the Norwegian food culture (Bugge, 2003). Scottish older consumers often described ready-made meals as 'junk' or 'rubbish' but considered them as foods that reduced the effort of preparation (McKie, 1999; McKie *et al.*, 2000).

Convenience in preparation is regarded as an important determinant of food choice (Costa et al, 2002; Scholderer and Grunert, 2005; Steptoe *et al.*, 1995; Rappoport *et al.*, 1993). Even if time is more plentiful, the effort involved in obtaining and preparing food may be a relevant factor in the food choices of elderly. Studies among younger adults have demonstrated that increased efforts can affect food selection and can result in reduced intake (Meiselman *et al.*, 1994). Similar effects might be expected among older people especially in those who lack the skill to cook (Hughes *et al.*, 2004). The relationship between cooking skills and food choice is quite complex. It is often assumed that better or more comprehensive skills lead to more frequent cooking and the use of raw ingredients (Fieldhouse, 1995). The common barriers among older consumers to eating an adequate diet (e.g., vegetable food consumption) have been related to difficulties in eating as well as to the inability to prepare them (Dittus *et al.*, 1995). Segress Holmes and Gates (2003) found that preparation of vegetables hindered men getting adequate servings. In a study of older men living alone (Hughes *et al.*, 2004) it was found that men with good cooking skills reported better physical health and higher intake of vegetables. The study revealed that poor cooking skills and low motivation to change eating habits may constitute barriers to improving energy intake, healthy eating and appetite in older men. Other authors also suggested that sensory changes result in older adults eating less and restricting their food choices. A sensory impairment that occurs with aging can results in a consumption of a monotonous diet (Raats *et al.*, 1996; Rolls, 1992). Pelchat (2000) found that older subjects were more willing to try novel foods than younger adults (at least in a laboratory setting), attributing this finding to a reduction among the elderly in their ability to perceive unfamiliar/unpleasant aromas. Seniors are therefore at higher risk of consuming a

monotonous diet (Rolls and McDermott, 1991; Pelchat and Schafer, 2000). Easing the preparation of vegetable-based foods has the potential to increase vegetable intake and the use of products with convenience in preparation might potentially improve older people's diets. These 'meal solutions' might bring more healthy food choices for older consumers who have less strong cooking skills combined with a low interest in food-related activities such as cooking (Caraher *et al.*, 1999).

As well as effort in food preparation, the presence of physical disabilities, lack of enjoyment and skills in cooking may have implications for food selection and meal preparation among older people. Physiologic decline (e.g., sight, hearing, dental health) and other conditions may result in older people having related mobility problems thus not only finding it difficult to procure foods, but also to prepare them. This may result in restricted access to adequate amounts and types of food and subsequent inadequate nutrient intake (Keller *et al.*, 1999; Rovner and Ganguli, 1998).

27.3 Findings of the Food in Later Life Project concerning foods which ease meal preparation

Data from four qualitative studies, one of which is as yet unpublished (details of the data collection methods can be found elsewhere: Pfau *et al.*, 2005; Mattsson Sydner *et al.*, 2007; Saba *et al.*, 2008) within the pan-European Food in Later Life Project are used to illustrate older people's views on foods that ease food preparation. Data was collected in eight countries across Europe (Denmark, United Kingdom, Germany, Italy, Poland, Portugal, Spain, Sweden). The samples in each of the eight participating countries consisted of equal numbers of women and men, of each of two age groups (65–74 and 75 and older) and of those living alone and living together with a partner.

27.3.1 Problems and changes older people encounter during shopping and meal preparation

In each country 40 participants took part in an in-store interview and observation focussing on food procurement, followed by an in-home interview focussing on food preparation. Background data on all participants was collected through a set of questionnaires (Pfau *et al.*, 2005). The data reported in this section deals with the problems and changes older people encounter during shopping and meal preparation. Quotes from participants are used to illustrate the findings. In the case of quotes from German consumers, quotes are also taken from two further datasets from the pan-European Food in Later Life Project in which participants were also interviewed about the role food plays in their lives.

Across the studies of the Food in Later Life project participants associated good meals with being prepared with fresh foods.

'. . . what are the most important factors for you to make a good meal? – That it tastes fine, that it is freshly prepared and therefore not reheated' (German older consumer)

'I never buy pre-cooked products. I don't like them. People should be able to cook by themselves, a simple soup at least. When you buy pre-cooked meals, you never know how it has been cooked or prepared' (Spanish older consumer)

Primarily women who were healthy and had more time on their hands for cooking than they had prior to retirement now took more time to prepare meals and cook more elaborate meals. Participants in all countries mentioned having reservations about pre-processed foods, often based on a certain distrust of additives.

'Pre-cooked products are forbidden at home. We know they are not healthy, they have too many fats and colourings.' (Spanish older consumer)

'I buy sauerkraut . . . I don't know what is still in there. . . . Canned products are useful, when you are aboard a ship without any fresh food available, but I can buy some fresh food.' (German older consumer)

This corresponds with the results of a survey of European consumers (Eurobarometer, 1998) that reported that consumers viewed foods that were more processed to be less safe, i.e. frozen foods were regarded by 34% of respondents as 'unsafe'; canned products by 40%; other pre-packed products by 43%, ready made dishes by 49%.

But in all countries participating in the Food in Later Life Project respondents reported using more pre-processed foods than they had in the past, this was described as being in line with many changes to the food supply since the Second World War, i.e. more variety available, of higher quality and with better taste.

'It has changed as everything in the world is changing now. There are new . . . products, sauces, dried vegetables.' (Polish older consumer)

'Before the war there was nothing. A person had to prepare everything by self. Today everything is ready.' (Polish older consumer)

'There is a greater range of foods available and snack foods. There's more rice and pasta available although I don't like them. Milk has changed too, there used to be only full fat available. Fruit juices weren't available years ago and there wasn't any frozen veg available. We have frozen peas now, but we would like to have had a tin of peas when I was young.' (UK older consumer)

All in all, more pre-processed products were used, and not only as a reaction on health problems. One reason, for instance, was to get more time for other things.

'I usually buy can and tin products, they are more convenient: are easier and quicker to prepare.' (Spanish older consumer)

'Frozen courgettes flowers are ready-to-heat, I don't waste time when I prepare them.' (Italian older consumer)

'We buy ready to cook 'homemade' pasta, it is better, simple to cook, without dirtying the kitchen.' (Italian older consumer)

Similar results were found in a qualitative study (Bugge, 2003) where the use of ready-to-serve foods was an accepted alternative on those days when the importance of the meal has to be down-graded on account of other social activities. However, they didn't fall under the heading 'proper dinner', but rather are regarded as 'quick solution', and 'TV food'. Timesaving aspects or incapacity to cook were mainly the reasons of Dutch seniors for using ready meals, while reasons for not using them were related with a higher degree of trust and self-esteem achieved by preparing one's meal (Costa, 2003).

Participants ($n = 123$) in Germany completed an additional questionnaire about the types of food used for own meal preparation. Fresh food was primarily used for meal preparation for all types of dishes except pasta (Tables 27.2 and 27.3). People chose dried ready-to-cook products for pasta whereas dried products for soups and sauces belong to the category of ready-to-heat products which need fluid to be added and thermal treatment. Deep-frozen products seemed to be relevant for fish dishes (Table 27.2). One explanation for this may be the fact that the participants lived about 800 km away from the sea and fresh fish is thus not readily available (Table 27.3). Pre-processed foods are chosen less frequently for the preparation of meals, e.g. dried products for soups and sauces, deep-frozen products for producing soups, meat, fish and vegetable dishes (Table 27.3).

It was further found that choice and use of pre-processed food was often influenced by the fact that available products did not meet requirements, e.g. the

Table 27.2 Types of food most frequently used by a sample of German consumers ($n = 123$) to prepare different types of dishes

	Fresh food %	Chilled food %	Deep-frozen food %	Dried product %	Sterilized food %
Soups	**47.2**	0.8	**4.9**	**11.4**	**4.1**
Sauces	**40.7**	1.6	0.8	**12.2**	**3.3**
Meat dishes	**61.8**	**6.5**	**6.5**	0.0	0.8
Fish dishes	**42.3**	4.1	**26.0**	0.0	**4.9**
Vegetable dishes	**70.7**	0.8	**4.1**	0.0	1.6
Pasta, cereal dishes	10.6	0.0	1.6	**60.2**	0.8
Fruit dishes	**77.2**	0.0	0.0	0.0	**3.3**
Desserts	**34.1**	**9.8**	**8.1**	5.7	**4.1**

Question asked: 'What kind of food do you use most frequently for meal preparation?'

Table 27.3 Types of food less frequently used by a sample of German consumers ($n = 123$) to prepare different types of dishes

	Fresh food %	Chilled food %	Deep-frozen food %	Dried product %	Sterilized food %
Soups	4.9	0.0	**11.4**	**15.4**	**7.3**
Sauces	3.3	1.6	2.4	**11.4**	1.6
Meat dishes	1.6	2.4	**23.6**	0.0	0.8
Fish dishes	5.7	2.4	**11.4**	0.0	**6.5**
Vegetable dishes	0.8	0.8	**35.8**	0.0	3.3
Pasta, cereal dishes	8.9	0.8	0.0	4.9	2.4
Fruit dishes	0.8	0.8	3.3	0.0	**16.3**
Desserts	6.5	6.5	4.9	3.3	1.6

Question asked: 'What kind of food do you use less frequently for meal preparation?'

size and transparency of packaging. Barriers included package size being too large (multi-portions) for storage capacity (e.g., freezer compartment) or to be eaten in time to still be fresh (i.e., loss of freshness or left-overs would be spoiled) and packages were found to be too heavy to carry home.

'Here I can get smaller packages, for me alone this fits more, otherwise I have to throw away too much.' (German older consumer)

In some countries a certain degree of convenience is desired especially with regard to fresh vegetables and fruit. Bulk goods like cauliflower, cabbage or savoy are preferred in smaller units.

'Unfortunately I cannot eat as much as is the minimum purchase unit.' (German older consumer)

Costa (2003) also found consumers to express the wish for easy-to-open packages that keep meal components separated and allowed buyers to see the products inside.

It was evident that the extent to which pre-processed products were used was influenced by (a) participants' changes in the health status and (b) changes in living circumstances.

With increasing health problems, manual processing of foods (peeling, slicing) as well as the handling of manual and electrical equipment and the opening of different kinds of packaging caused difficulties. Not only the preparation process but also other related activities such as dishwashing, cleaning and tidying up were considered strenuous and too exhausting. There was thus a need for simplification or reduction in meal production, including a decrease in the variety of dishes included in an individual's diet. The more participants' health was impaired, the higher the level of processed foods being used. In the past, products such as bread and cheese were bought as unsliced, now being replaced by sliced versions of the products, and the mincing of meat

was left to the butcher. Formerly homemade dishes prepared from a variety of ingredients were now bought as 'convenience' products or replaced by other or similar dishes.

'I ask my husband to unscrew lids of jars. I buy ready to cook puff pastry because my hands hurt.' (Italian older consumer)

'I bought Italian bread at the baker's. I don't bake as much bread as I used to.' (Danish older consumer)

'I don't prepare Spätzle as often as I did formerly'. . .'You prefer to buy them?' . . .'No, I don't – but macaroni or something like that, yes, macaroni and noodles, yes.' (German older consumer)

With regard to vegetables there was an increased reliance on deep-frozen products, ready for further use in the kitchen. Use of these products enabled participants to at least season foods according to their own taste preferences, an often mentioned issue regarded as being important. This confirms findings of Costa *et al*. (2002) that elderly prefer playing at least a small part preparing their meals, as this increases feelings of self-reliance and control over what is eaten.

Side dishes formerly made using basic ingredients are replaced by dried or chilled ready to reheat products. The methods of preserving or conserving foods (e.g., home-made jam) are used less and less, and certain preparation methods are abandoned altogether (e.g., baking bread and cakes).

'ehm you told me that you had baked many more cakes formerly' – 'Yes' – 'And you don't do it any longer?' – 'Not at all.' – 'You buy it ready-to eat?' – 'Yes, I have a deep-frozen one, that is the cheese cake . . . and there is a cake shop, which has good cakes. Sometimes we get some when we feel like it . . . I have baked a lot, you know how much I have baked – I gave it up completely, for me the preparing is still very strenuous.' (German older consumer)

'Previously I prepared vegetable salad more often, and now I do it rarely. Previously I often baked cheesecake and I don't do it anymore.' (Polish older consumer)

Changes in living situation had a severe impact, sometimes leading to extreme changes in meal preparation and consequently in food choice and diet. Men with little or no cooking skills experienced the greatest changes in meal provision after the death of their wives. In some cases they tried to increase their cooking skills by attending cooking courses and/or going out to eat more often than in the past. Some tried to minimize the effort needed for preparing meals through using a wide variety of pre-processed food of different convenience classes. But primarily they selected their own combination of pre-processed food items and not full meal replacements – often for use with a microwave oven. In these cases, the variety of meals was reduced when compared with the past when

their meals were provided by their wives. However, men who were able to cook and could prepare dishes 'from scratch' preferred fresh foods, especially in respect to meat, fruit and vegetables. In some cases (primarily women) the loss of the partner led to the feeling that self-production of meals is 'not worth the effort just for myself'.

'. . . but on principle I don't take a ready-to-eat meal, right, very seldom, there is an exception here and there, right, perhaps a soup or so but in the whole I don't take a ready-to-eat meal.' (German older consumer)

'Well sometimes the amount of effort that has to go into doing something like that for one person, it takes an awful lot of time and when there are alternatives available.' (UK older consumer)

In conclusion, the results of the Food in Later Life Project show that older people have developed strategies for simplifying meal preparation. Strategies such as elimination (foods formerly consumed are no longer eaten), substitution (self-prepared dishes are replaced by pre-prepared foods) and modification (use of similar food prepared by a different preparation method) are particularly used to simplify preparation and reduce effort. Applying such strategies allows older people to retain their independence with regard to meal provision. These types of strategies mirror those outlined by Sobal *et al.* (2006) as being ways of simplifying food choices. Simplification of meal preparation is likely to have an impact on food choices.

Quantitative data obtained from respondents described by Mattsson Sydner *et al.* (2007) show (Fig. 27.2) that those with increased levels of health impairments attach greater importance on ease of food preparation. These results are

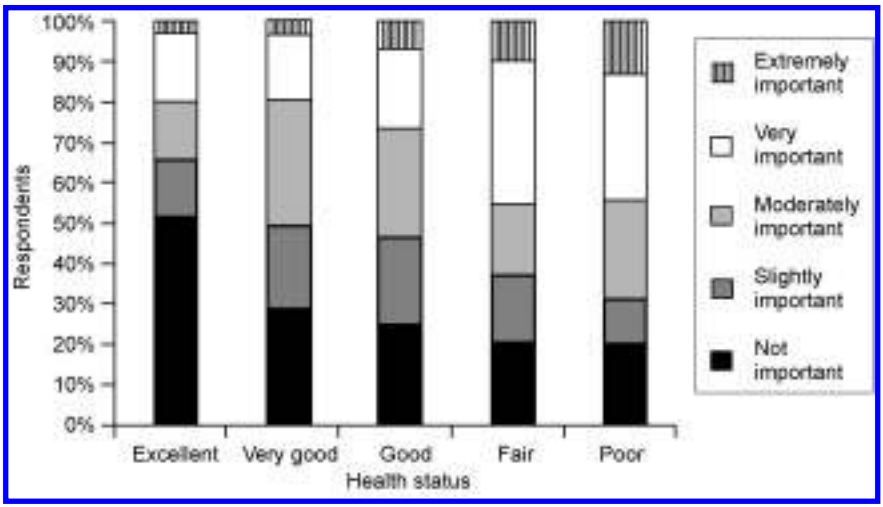

Fig. 27.2 The importance of easy to prepare foods to older people of varying health status ($n = 611$).

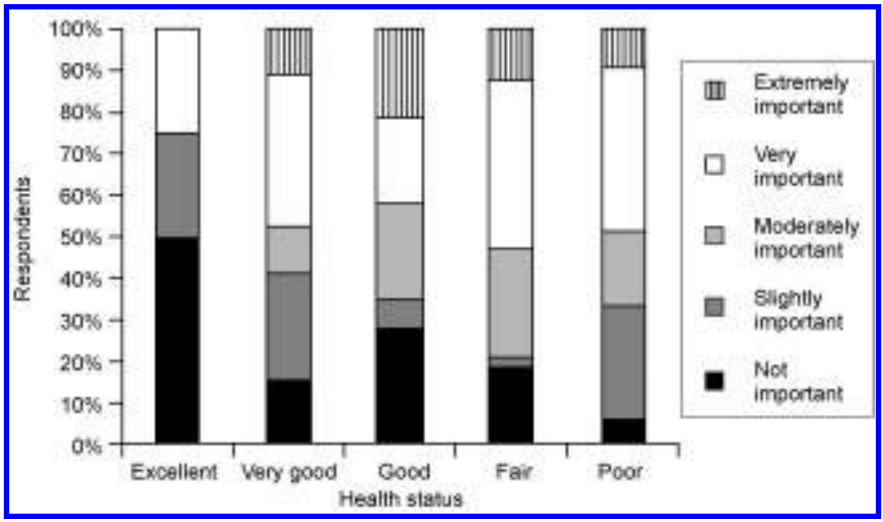

Fig. 27.3 The importance of easy to prepare foods to people who are users of meals on wheels or meals of day care centres and varying in health status ($n = 157$).

mirrored in a sample of older people who are users of meals on wheels or meals of day care centres (Fig. 27.3).

But the results of this study show, too, that the use of complete ready-to eat meals was put off as long as possible; rather utilised were pre-processed food items.

'Did you get deep-frozen meals or something like that delivered then?' – 'Deep-frozen meals, no! We take sometimes deep frozen vegetables from a delivery service but not complete meals.' (German older consumer)

'. . . that I get things delivered by a delivery service, but ready to reheat meals are not the rule, also rather croquettes are wonderful.' (German older consumer)

Especially people with increasing health problems, who were used to cooking meals using fresh ingredients, seem to have a pattern for how they integrate the use of convenience products. With increasing problems concerning meal preparation, an increasing use of pre-processed food could be observed. Components of the menu which cause problems during preparation are replaced by products less labour-intensive and with fewer requirements concerning cooking skills. At the beginning only pre-processed food items are chosen, e.g. fresh or deep frozen cut vegetables, which need to be seasoned and cooked, later this component is replaced by ready-to-reheat vegetables. Often the meat or fish component is a ready-to-reheat item (chilled, canned or deep-frozen) and the side dishes like rice, pasta, potatoes or salad are prepared by the older person themselves. An incremental increase from pre-processed food items to complete home-meal replacements with highest levels of convenience can be observed.

In spite of pre-processed foods not meeting all requirements and desires, these products were accepted if their use kept people independent and enabled them to stay in surroundings they were used to.

27.3.2 Attitudes towards ease of preparation in selected European countries

In a further study within the pan-European Food in Later Life Project, a sample of 768 older consumers across eight European countries (Denmark, Germany, Italy, Poland, Portugal, Spain, Sweden and United Kingdom), was interviewed to investigate perceptions, preferences and attitudes towards convenience in preparation of vegetable soups (Saba *et al.*, 2008). In each country, a range of seven vegetable soups was identified, five of which varied in readiness to eat and convenience of packaging and storage, and two represented by a selection of mixed fresh vegetables in season requiring full preparation (to be washed, peeled and cut; i.e. 'no convenience') and a selection of cut mixed fresh vegetables in season (to be washed; i.e., 'low convenience'). The first part of the interview (in-depth interview) was carried out by using the Repertory Grid Method, an effective method to describe perceptions of foods using consumers' own language.

Overall, the products were perceived in a similar way across countries. Older consumers tended to describe consumption-ready vegetable soups mainly by making associations related to preparation, rather than on their own preferences and evaluations, a finding echoed in literature (Worsley, 1980; Axelson *et al.*, 1986). Conversely, fresh vegetables requiring full preparation or considerable preparation (cut fresh vegetables) were mainly associated with abstract constructs such as, *taste*, *freshness*, *health*, *familiarity*. The lack of attributes describing preference and evaluations associated with ready-to-eat vegetable soups on the one hand would indicate that those kinds of foods are purchased to reduce the effort of preparation and regarded as a last resort when the 'fresh' alternative is not a practical physical option (McKie, 1999; McKie *et al.*, 2000). On the other hand, this finding would confirm the hypothesis that the more an individual can enjoy taste, the more this person will be inclined to invest time and energy in activities that provide this sensation (Candel, 2001; Chapter 5 by Fjellström in this book). Furthermore, this result would suggest that even if time may be more plentiful, the effort and energy involved in preparing meals may still be important (Hughes *et al.*, 2004; Meiselman *et al.*, 1994).

However, some minor differences were observed across countries. Taste was not found to be important for Danish and British seniors, showing that sensory attributes might be not important in driving choice of vegetables to prepare soups in these countries. German seniors appeared to have a more negative perception of products with convenience in preparation. In particular, ready meals were associated with 'additives'. Furthermore, they were described as products that give the possibility of choosing how to prepare the meal in Sweden, Germany, and Denmark. On the whole, the variable price was not

found to be a relevant attribute associated with those products, even if mixed fresh vegetables were regarded as 'inexpensive products' in Sweden. Previous research didn't find the price to be an important attribute, and suggested that older consumers expected to pay more for the service provided with ready meals (Costa, 2003).

Pleasure associated with performance of the behaviour was the most important determinant of intention to eat convenience foods in Germany, Denmark and Sweden. Perceived need was the most important factor in determining the intention to eat convenience foods in the United Kingdom, Poland and Portugal. Perceived control and subjective norms were the most important factors influencing the intention to eat convenience foods in Italy. The encouragement of consuming 'ready-meals' might represent an opportunity to have healthier food choices and to reduce the risk a monotonous diet for older people who cannot or do not know how to cook, combined with a low interest in food-related activities such as cooking.

The second part of the interview was based in part on the Theory of Planned Behaviour (see Table 27.4). A component measuring the extent to which it is felt necessary to eat convenience foods (perceived need) was assessed as well. Generally speaking, in this European study older people were found not to view consuming convenience foods positively. They also did not feel the need to consume these products nor did they have the intention to consume them. Their average ratings of attitude, subjective norm, perceived control, perceived need and intention were, in fact, quite low (= 3.6) in all countries (Table 27.4). On average, older (75 years and older) respondents tended not to perceive a social pressure towards a behavioural intention to eat convenience foods in each country, especially in Spain, Germany and Denmark. Intention to eat convenience foods was very low in all countries, especially in Portugal and Spain. These findings would suggest that a possible intervention to increase consumption of convenience foods among older population should include strategies aimed at increasing their positive attitudes and perceived need of those foods (Chapter 5 by Fjellström in this book).

27.4 Future trends

The elderly are likely to become an increasingly important market sector. There is already a clear recognition that this group is worthy of attention, understanding and effort (Burt and Gabbot, 1995). It is important to keep in mind that the elderly do not form a homogeneous group (Moschis *et al.*, 1997) and that the mature consumer market is constantly changing. Uncles and Ehrenberg (1990) highlighted the need to distinguish between the active older consumers whose requirements are similar to when they were younger, and the frail elderly or oldest old with their constrained shopping and eating habits. Further it is well known that chronological age may not be a good discriminator of older consumers who age differently and at different rates (Moschis and Mathur,

Table 27.4 Mean ratings and standard deviation (in parenthesis) for the variables: Attitudes, Subjective norms, Perceived behavioural control, Perceived need and Intention to buy convenience foods, by each country

Component	Question	Italy	Spain	Portugal	Poland	Germany	Denmark	Sweden	UK
Affective attitude	How unenjoyable or enjoyable would it be for you to eat convenience foods in the next month? (Scale: 1 = extremely unenjoyable to 5 = extremely enjoyable)	3.14 (1.24)	2.43 0.96)	2.48 (1.28)	3.04 (1.06)	2.85 (1.12)	2.92 (1.34)	3.16 (1.07)	3.15 (0.91)
Cognitive attitude	How harmful or beneficial would it be for you to eat convenience foods in the next month? (Scale: 1 = extremely harmful to 5 = extremely beneficial)	3.09	3.06	2.61	2.91	2.98	2.96	2.88	2.99
Subjective norm	People who are important to me think I should eat convenience foods in the next month (Scale: 1 = strongly disagree to 5 = strongly agree)	2.61 (1.16)	1.93 (0.88)	2.46 (1.00)	2.85 (1.22)	2.16 (1.03)	1.81 (1.19)	2.26 (1.05)	2.10 (0.96)
Perceived behavioural control	How easy or difficult would it be for you to eat convenience foods in the next month? (Scale: 1 = extremely difficult to 5 = extremely easy)	2.94 (1.25)	3.57 (0.54)	2.65 (1.49)	3.15 (1.20)	3.38 (1.17)	3.64 (1.22)	3.38 (1.04)	3.61 (0.99)
Perceived need	To what extent do you feel that you need to eat convenience foods in the next month (Scale: 1 = definitely do not need to; 5 = definitely need to)	2.80 (1.24)	1.42 (0.99)	1.78 (1.36)	2.49 (1.42)	2.05 (0.90)	1.96 (1.07)	2.18 (0.93)	2.35 (1.25)
Intention	Do you intend to eat convenience foods in the next month? (Scale: 1 = definitely do not intend to; 5 = definitely intend to)	2.80 (1.24)	2.00 (1.39)	1.87 (1.40)	2.47 (1.42)	2.48 (1.24)	2.60 (1.48)	2.89 (0.93)	2.94 (1.36)

1993). It may be argued that age should be an increasingly irrelevant segmentation variable and behavioural and life-style characteristics of different groups are more important (Szmigin and Carrigan, 2001).

By producing easy-to-prepare, enjoyable foods, the industry might better meet the nutritional needs of elderly people. A changing variety of small packs of convenience foods, easy to open and store, at reasonable cost, with acceptable flavour and texture will help elderly in regularly eating healthy and tasty meals. In the product development of ready-made dishes, an increased focus on enhanced taste will be worthwhile for the food industry, and older consumers will get more pleasure out of their food. The need to provide user-friendly packaging and legible labels is especially important to older consumers, who may have limited dexterity, hand strength, and visual acuity compared to younger adults. The encouragement of consuming 'ready-meals' might represent an opportunity to have more healthy food choices and to reduce the risk a monotonous diet for older people who have insufficient cooking skill combined with a low interest in food-related activities such as cooking (Caraher *et al.*, 1999). One might expect that ensuring that foods are available in a range of different classes of convenience will better enable people at risk of becoming dependent due to health status and other factors, to care for themselves for much longer. It will also be important to study whether the older people of the future prepare and consume foods in the same way as the older people of today.

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28

Designing new foods and beverages for the ageing

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Abstract: This chapter shows how a consumer-led approach to product development can be employed in the design of new foods and beverages for the ageing. After a brief description of the underlying concepts and practices, a detailed picture is given of how this approach was used in the design of home meal replacements for senior households. The chapter also includes a comprehensive review of the main determinants of food preference and meal choice behaviour at a later age.

Key words: new product development (NPD), home meal replacements (HMR), ready meals, food choice, senior consumption behaviour.

28.1 Introduction

Doubled-dipped spicy chicken, blue cheese and walnut salad with maple dressing, and chocolate-dipped bananas – for whom do you think this menu is designed? A hungry teenager perhaps? Think again! These are Rachel Ray's recipes for self-standing seniors (The senior corner, 2006). Today's seniors – and, most importantly, tomorrow's – are an ever-increasing, highly diverse group of people wanting to live a healthy and fun life as much as any other. And like everybody else, they increasingly see how important it is to eat healthy and delicious food in a pleasant environment to achieve just that (Roberts, 2002). However, to maintain the right balance between enjoyable food, a healthy diet and a pleasant lifestyle is perhaps harder on the ageing than on any other demographic group.

Generally speaking, the food industry has been slow in transforming the wealth of available knowledge regarding the nutritional needs and sensory

perception of the ageing into new food products (Roberts, 2002). Although seniors are probably more willing to try new foods than previously thought (Pelchat, 2000; Otis, 1984), highly tailored approaches are still required for new products to succeed, given the heterogeneity and special requirements of this group (Fillion and Kilcast, 2001; Herne, 1995; Kremer *et al.*, 2007; O'Donnell, 1994; Roberts, 2002; Rolls, 1993; Russel *et al.*, 1999; Wysocki and Pelchat, 1993). Moreover, to position new products to target the ageing market is a notoriously difficult task, as foods labelled 'for seniors' will probably turn out to be fairly unattractive for old and young alike (Roberts, 2002).

This chapter shows how the design of new foods and beverages for an ageing population can be tackled through a consumer-led approach to product development. After a brief description of the underlying concepts and practices, a detailed picture is given of how this approach was used in the design of home meal replacements for senior households. The chapter also includes a comprehensive review of the main determinants of food preference and meal choice behaviour at a later age. Finally, relevant implications are derived from the work presented and future trends in the technological development of foods for the ageing are highlighted.

28.2 Consumer-led new product development: the concept and process in the food and beverage industry

The concept of consumer-led new product development (NPD) was introduced in the early 1990s by Urban and Hauser (1993). It refers to a market-oriented innovation strategy that uses consumer needs as the basis for the development of new products with added value. Despite the promptness with which several marketing and engineering experts advocated the employment of this strategy in the food and beverage industry (Lord, 2000; van Trijp and Steenkamp, 1998), it was not until recently that concrete guidelines for its practical implementation were supplied (Costa and Jongen, 2006).

Figure 28.1 depicts the key implementation stages of a consumer-led NPD process in the food industry. The *opportunity identification* stage aims at defining the target markets for the new foods, as well as generating product concepts that can successfully compete in these markets. At this stage, supported by a thorough understanding of the competitors' and their own core competences and unique strengths, companies should conduct a strategic assessment of which food technology platforms might provide a solid basis for product development. If, given the outcome of such an assessment, potentially attractive markets and concepts can be found, the decision to initiate the development process can take place (Dahan and Hauser, 2002a; Robinson, 2000; Urban and Hauser, 1993; van Trijp and Steenkamp, 1998).

The *design* stage seeks to identify the key consumer benefits the new food is to provide, as well as the positioning of these benefits *via-à-vis* the competition. It is thus throughout the different phases of this stage that the development of the

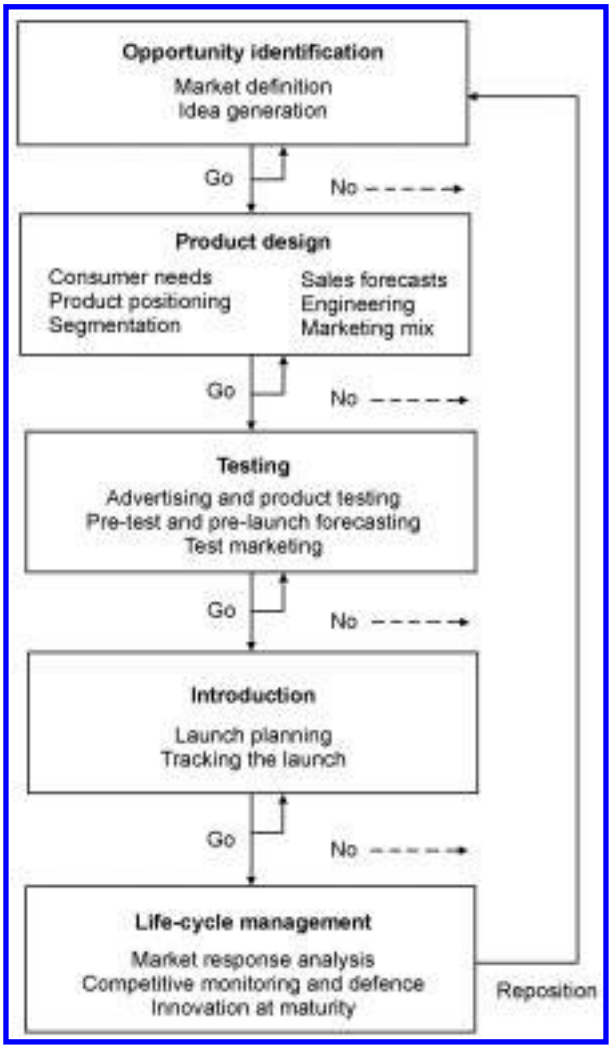

Fig. 28.1 The consumer-led new product development process (Costa and Jongen, 2006).

physical product, the corresponding marketing strategy and the service policy takes place. The strategic information about the target consumers collected during the opportunity identification stage serves as the primary input for the first design phase – *opportunity definition.* At this point, the potentially rewarding concepts earlier selected are submitted to the target consumers' evaluation. Such an early evaluation is crucial, since it allows for an assessment of the market potential of the selected ideas to take place before any considerable funds are committed to the development process. Qualitative research methods are usually employed first to identify relevant issues which may need further investigation, while quantitative methods are used at a later time to

establish the expected benefits and their relative importance in a more precise manner (Urban and Hauser, 1993; van Trijp and Steenkamp, 1998).

Means-end chain theory (MEC), through its most usual research application – the performance and analysis of laddering interviews and the generation of the target consumers' hierarchical value maps (Gutman, 1982; Hinkle, 1965; Olson and Reynolds, 2001) – can be a very helpful tool in the early design phases of a consumer-led food product development process (Costa *et al.*, 2004). MEC provides a more precise definition of food consumption motives by depicting how perceived product attributes are linked to self-relevant consequences of consumption (the key benefits) and personal life values (or goals), in a hierarchical model of consumers' cognitive structures. This model is thus able to pinpoint the potential choice criteria used by consumers to evaluate and select among alternative products or services, and explain the higher-order reasons leading to the relevance of these particular criteria. This results in the generation of three types of useful information about the target market (Audenaert and Steenkamp, 1997; Grunert and Valli, 2001; Gutman, 1982; Olson and Reynolds, 2001; ter Hofstede *et al.*, 1999; van Trijp and Steenkamp, 1998):

- The key benefits consumers expect from foods, which can be used to determine the positioning of new products in the marketplace;
- The attributes of food products consumers use to infer the delivery of key benefits (and the absence of negative outcomes or risks) associated with consumption, which can provide guidance to later R&D endeavours;
- The values and goals determining the relevance of the different benefits to consumers, which can be used to design and target advertising campaigns for the launch of new products.

A list of consumer benefits and their relative importance is then conveyed into a *refinement* phase, in which the new product starts to take shape. This is achieved through a careful analysis of the relationships between consumers' food perceptions, preferences and choices, on one hand, and the product's potential technological features on the other. Underlying this analysis is a model of food consumption behaviour, in which preferences are formed based on the perceptions of the products' features and lead, in turn, to choices contingent upon price and availability (Urban and Hauser, 1993; van Trijp and Steenkamp, 1998). When the refinement phase is successfully completed, i.e., when it was possible to design a new food that can potentially fulfil consumer needs in a superior and unique way, the assessment of the proposed design takes place in the *opportunity evaluation* phase. This assessment consists of forecasting sales for the new food product based on the aggregation of the probabilities of individual consumers' preferences and choices (Urban and Hauser, 1993).

Further development and testing of both the new product and its marketing strategy occurs when the forecasted market performance meets company targets. Once the t*esting* stage has been successfully concluded, *market introduction* can take place. The monitoring of the target consumers' and the competitors' reactions to the introduction, which may lead to further adjustments of both

product and marketing strategy, constitutes the final stage of the development process, the so-called *life-cycle management* (Urban and Hauser, 1993).

A consumer-led food product development process, such as the one just described, simultaneously reflects and confers concrete substance to the main themes of a market-oriented innovation strategy (Costa *et al.*, 2000; Costa and Jongen, 2006):

1. The needs of the targeted consumers are the starting point of the product development process, with their assessments of ideas, concepts, prototypes and products *vis-à-vis* those of competitors directing the underlying managerial decision process from onset.
2. The primary role of technological development is to support the fulfilment of consumer needs and the creation of market value. As such, the decision to adopt a specific technology platform is based on its forecasted ability to generate new products that deliver superior consumer value relatively to those already existing in the marketplace.
3. To be able to not only match the right market with the right technology but also ultimately deliver the product in accordance with the target consumers' requirements, a process of translating consumer information (needs, perceptions, preferences) into technical features (technological parameters, product specifications, quality characteristics) must continuously take place.

Throughout the following section of this chapter, a research study illustrating the application of consumer-led food product development in the generation of new home meal replacements (HMR) for an ageing target market will further highlight these central themes.

28.3 Consumer-led food product development for the ageing: the case of home meal replacements

28.3.1 Identifying opportunities

Target market

Senior citizens (55 and over) currently represent 23% of the Dutch population, a share expected to rise to about 30% in 2015, mostly due to an increase in life expectancy (CBS, 2000a,b). The majority of Dutch seniors are at least in reasonable health and have an income from which they can live comfortably, though a considerable minority – some single seniors and widows, the very old and seniors from ethnic minorities – find themselves in a less favourable situation (Klerk and Timmermans, 1999). Nonetheless, it seems that most Dutch seniors will be enjoying the rest of their extended lives with a reasonable degree of both individual and economic independence. These circumstances, by means of creating the expectation of a growing 'grey' buying power with a desire for quality products and services, have made of this group a very attractive target market for many companies in Europe (Hielkema and Kuyer, 1995).

As Dutch seniors become more and more active in society, they will have

increasingly less time and energy left for domestic chores. Consequently, they will also start questioning themselves about what they will eat when they are no longer willing or able to purchase and prepare their own meals, and yet must for a great deal remain self-sufficient (Hielkema and Kuyer, 1995). When this happens, it seems reasonable to expect that seniors will increasingly demand solutions that can conveniently and satisfactorily replace their own cooking (Roberts, 2002). The question is, what will they be looking for and where will they be able to find it?

Figure 28.2 depicts the multi-stage decision-making process underlying consumers' choice of meal solutions (Costa *et al.*, 2004). This consumer-oriented approach to product-market structure analysis (Srivastava *et al.*, 1984) can be used to better understand how the different segments of the Dutch senior population choose between alternative types of meals. According to a life-style segmentation of Dutch seniors (Sonneveldt, 1996), about 20% of these are reasonably healthy, well-off widows – the so-called *Silvered Singles* – who are very active in associations and clubs and therefore eat out frequently in restaurants, hotels and catered events. Representing another 20% of this target market are the *Golden Enjoyers*, socially and physically active people with high spending power and not much will to cook everyday. Although eating out often, these seniors still appreciate staying at home to receive relatives and friends, or simply to relax and enjoy their houses. Finally, the majority of Dutch seniors are considered to be *Bronzed Home-Birds*, conservative ageing citizens with diminishing health and little wish to be socially active, who are keen on cooking and eating traditional Dutch meals. It seems that for at least the last two segments, though likely in a very different manner, the development of new meal solutions to be consumed at home could constitute an attractive market opportunity.

Strategic assessment and product concept

At the core of market opportunity identification lays the strategic assessment of which technology platforms may provide a solid basis for the development of new food products with superior value for the targeted consumer group. Such an assessment is essentially based on an overview of the benefits delivered by existing products and their underlying technological structure. Importantly, this overview should contribute to the identification of structural gaps, indicating where benefits are being demanded by target consumers but not delivered by any of the existing products and technologies, since these constitute the development opportunities. Finally, it should also facilitate an early and relatively simple appraisal of the relative worth of the different development opportunities it generates (Cooper and Kleinschimdt, 1986; Dahan and Hauser, 2002a; Urban and Hauser, 1993).

Home meal replacements (HMR) are manufactured main courses (or pre-assembled main course components) – containing a protein (animal or plant) and a carbohydrate (starch) source, as well as a vegetable component – designed to fully and speedily replace the main course of a home-made meal (Costa *et al.*,

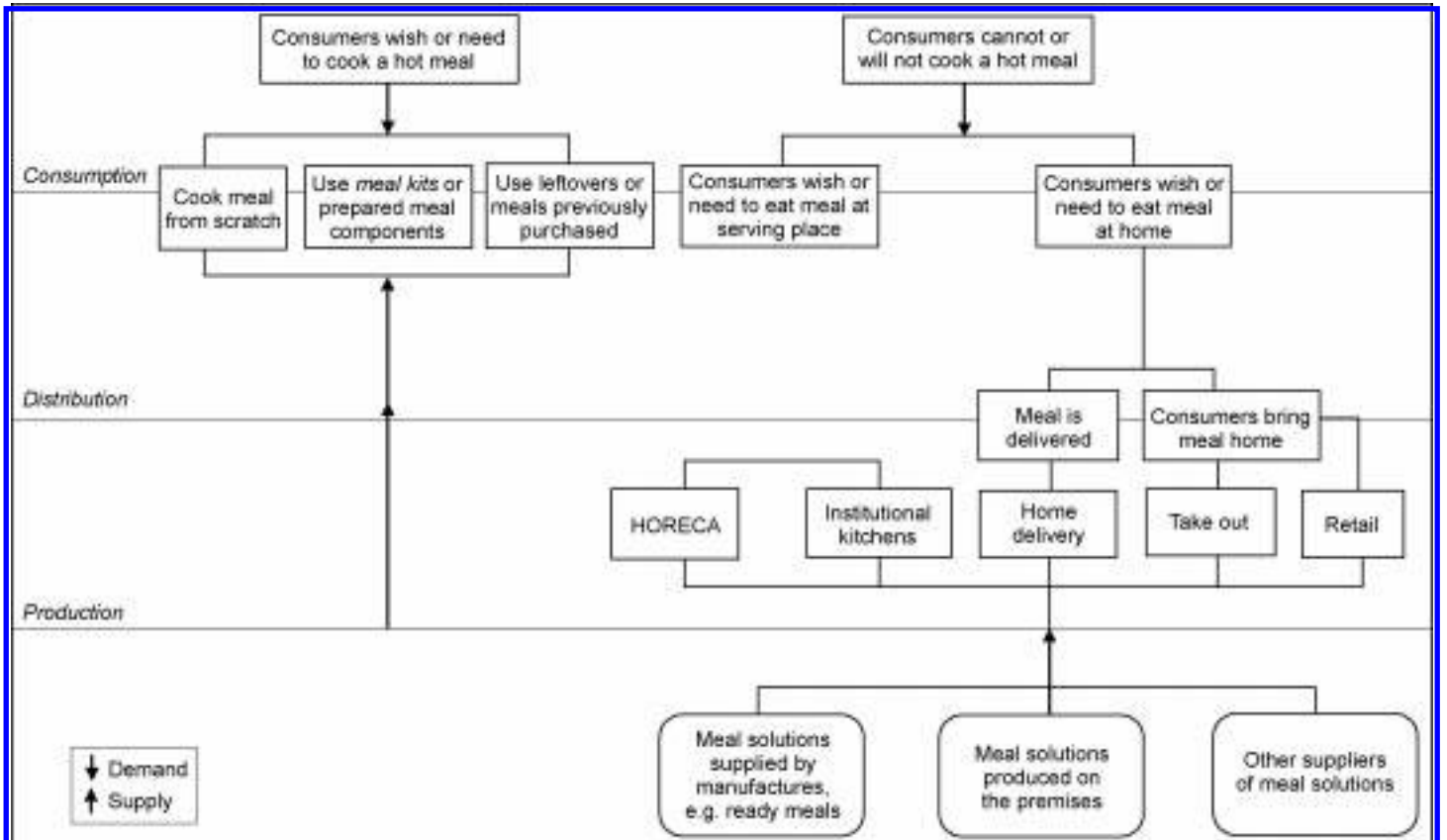

Fig. 28.2 The multi-stage decision-making process underlying consumers' choice of meal solutions (HORECA: HOtels, REstaurants and CAtering) (Costa *et al.*, 2004).

2001a). This category encompasses not only pre-packed meal courses sold by food retailers, the so-called ready meals, but also meal solutions supplied through services like take-out, home delivery and meals-on-wheels, and corresponds roughly to the area on the right-hand side of Fig. 28.2. Consumers' selection of meal replacements can be determined by several of the products' specific attributes, such as taste, similarity to homemade, main ingredients or freshness. Nevertheless, it is their distinctive convenience features and the relative level with which they are present that determines consumers' choice both at category and at product level to a large extent. Importantly, these features are also directly linked to well-defined technological processes (Dade, 1992; Datamonitor, 2003; Ritson and Hutchins, 1995; Steptoe *et al.*, 1995; Swoboda and Morschett, 2001).

Table 28.1 presents an overview of the benefits delivered by existing and potential HMR products, structured around two main dimensions – convenience in storage and convenience in preparation – both containing four levels of increasing convenience (Costa, *et al.*, 2001a). Each cell entry depicts the percentage of senior respondents (55–94 years old) from the Dutch National Food Consumption Survey 1997–98 (DNFCS) who consumed products delivering the respective level of combined convenience. These figures indicate a concentration of HMR consumption at the time in two convenience levels – ready to eat products with minimum shelf-life, mainly prepared meals supplied by the foodservice sector, and manufactured meal solutions with long durability but which require a more or less prolonged heating before consumption.

When compared to the overall sample of HMR consumers from the DNFCS (Costa *et al.*, 2001b), the target market exhibited a relatively lower preference for products with the highest convenience in preparation and a relatively higher preference for HMR with a very long shelf-life. This could be associated with perceived time scarcity and easiness in regular food procurement on behalf of the younger consumers relative to their senior counterparts. There was also a relevant difference in terms of the specific product selection. While both the seniors and the overall population consumed mostly take-away Oriental meals and canned meal soups, frozen traditional Dutch dishes were relatively more preferred by older respondents (especially those older than 65), with younger

Table 28.1 Overview of the percentage of senior respondents (55–94 years old) from the DNFCS that consumed HMR products in each level of combined convenience in storage and in preparation ($n = 121$)

	Ready to cook (%)	Ready to end-cook (%)	Ready to heat (%)	Ready to eat (%)
Shelf-life < 1.5 weeks	0	0	6	26
1.5 weeks ≤ shelf-life <1.5 months	0	0	7	8
1.5 months ≤ shelf-life < 1.5 years	0	11	15	0
Shelf-life ≥ 1.5 years	0	5	22	0

ones eating mostly frozen pizzas instead. This could indicate a relatively higher preference of the target market for products that closely mimic traditional home-made meals, a hypothesis which finds support in findings from other consumer studies (Herne, 1995; Laureati *et al.*, 2006; Sonneveldt, 1996).

Importantly, the overview depicted in Table 28.1 highlighted relevant mismatches in the way the assortment of manufactured HMR products commercialised at the time was meeting the demand of the target group. Such mismatches could be converted into potentially rewarding development opportunities. Though seniors clearly preferred manufactured products the preparation of which involved a fair amount of cooking, few such products could be found on offer. This was mainly because earlier R&D and marketing efforts of ready meals' producers had been directed mostly towards younger consumers. Moreover, the concurrent seniors' trend to favour products with a very long shelf-life posed interesting challenges to the development of new processing technologies. This was namely the case for technologies that could produce high durability meal replacements made of raw or minimally processed ingredients. Finally, this outcome stressed the need for manufacturers to address the general trend to seek meal solutions in take-out or home delivery services. This could be done through either the development of short-life retail products competing on readiness for consumption or of prepared meal components for the food service sector.

28.3.2 Designing the new product

Opportunity definition

The potentially rewarding product concepts and technological developments identified in the previous stage must be submitted to the target market's evaluation as early as possible in the design process. Such evaluations usually start with qualitative consumer research studies, like focus groups and personal interviews (Krueger and Casey, 2000; Marshall, 1997). These aim at the timely detection of all the potentially relevant strengths and weaknesses of the identified concepts for the targeted consumers, as well as perceived bottlenecks and synergies which could turn out to affect the development and acceptance of innovative technologies. Subsequently, semi-quantitative and quantitative research studies are envisaged with the aim of defining more precisely the aspects previously uncovered and, most importantly, establish their relative importance for the target group (Costa and Jongen, 2006; Urban and Hauser, 1993; van Trijp and Steenkamp, 1998, van Kleef *et al.*, 2005).

In the context of a research project on the development of HMR for the ageing, four focus groups ($n = 32$) and 11 individual, in-depth interviews were conducted with target consumers (54–84 years old, 90% retired, 45% living in single-person households (Costa, 2003; Costa *et al.*, 2002). The aim of these qualitative studies was to ascertain the target market's general views on meals and meal solutions, as well as its evaluation of some specific meal replacement products and the benefits delivered by them, given that very little was known at the time about these topics. Subsequently, with the goal of establishing the

relative importance of the motivations behind meal choice in a more precise manner, 25 individual laddering interviews were conducted with target consumers (55–87 years old, 85% retired, 45% living in single-person households) regarding both meal solutions in general and specific HMR products (Costa *et al.*, 2007). Finally, to be able to forecast which of the relevant motives behind meal choice would have the strongest impact on the target market's demand for different HMR products, a target consumers' sample ($n = 112$, 55–85 years old, 70% retired, 15% living in single-person households) was surveyed regarding its meal preparation behaviour and related attitudes (Costa, 2008a). All senior consumers participating in the research project were self-standing Dutch citizens in charge of meal acquisition and/or preparation at their households (about 80% women), and included both HMR users and non-users in an equal proportion.

Target consumers' evaluation of home-made meals

The most striking outcome of the qualitative research performed was the high personal relevance given to the consumption of home-made meals. This had, in turn, a strong impact on the target market's evaluation of other meal solutions. Full hot meals were reported to be prepared and eaten daily on weekdays, mainly in the evening. These meals were said to be essentially composed of one main course – usually stewed or fried meat with gravy, boiled potatoes and boiled vegetables – often, but not necessarily always, accompanied by soups and salads, as starters or side-dishes, and a dairy-based dessert. Resembling preferences in several other North European countries (Fjellström *et al.*, 2001; Herne, 1995; Marshall, 2000; Prättäla, 2000), 'meat and two vegetables' courses constituted simultaneously the most typical and the most favoured centrepiece of a cooked dinner. On weekends, however, target consumers indicated that they were less willing to cook and rather ate soups and sandwiches (or salads in the warmer months), order meals from the Chinese or Italian take-out or went out for dinner.

Figure 28.3 depicts the target market's hierarchical value map of the preparation and consumption of home-made meals on weekdays. Accordingly, the main features of a cooked dinner in an ageing Dutch household are simplicity (i.e., prepared with few ingredients and seasonings and basic, time-saving cooking methods), tastiness, diversity (i.e., main ingredients changing from meal to meal), freshness (i.e., prepared everyday from scratch with unprocessed foods) and safety. The last two features are related not only with the use of fresh, organically produced ingredients (perceived as being more natural and pure), but also with home-made meals being the outcome of household processing rather than manufacturing. Simple cooking, good sensory quality and healthiness have also been identified as playing a major role in seniors' choice of foods and meals in similar studies (Krondl *et al.*, 1982; Laureati *et al.*, 2006).

Target consumers viewed preparing their cooked dinner as a mandatory and essential part of their daily routine, to be kept tightly under their own control. However, cooking could also be fun, especially if there was the opportunity to try out new recipes from magazines or retail brochures. These reportedly

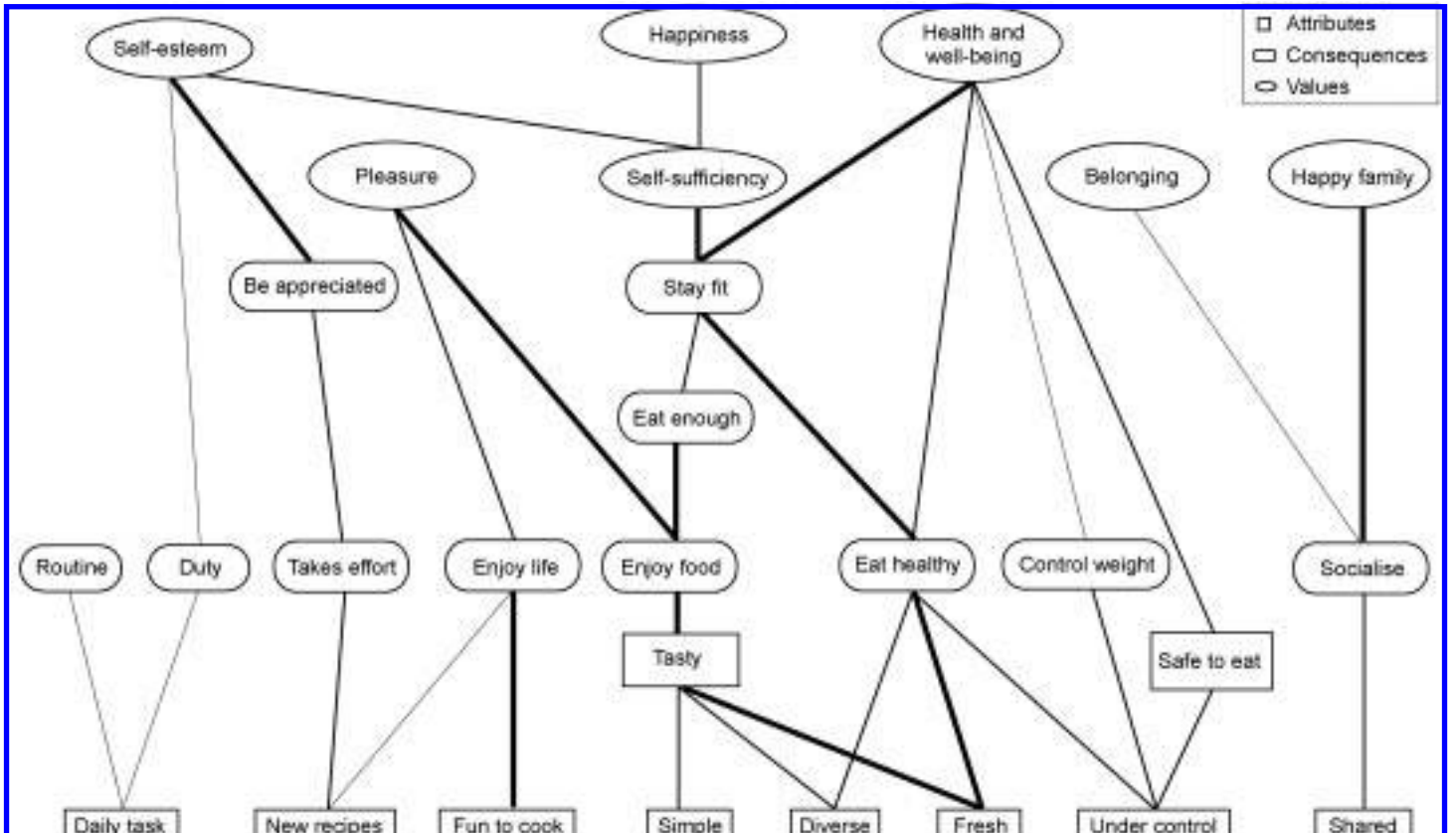

Fig. 28.3 Seniors' (55–87 years old) hierarchical value map of the preparation and consumption of home-made meals on weekdays ($n = 25$). The thickness of the connecting lines indicates the strength of the associations between the cognitive elements.

introduced new ingredients and flavours that offset the monotony of the typical Dutch diet and helped avoid boredom and lack of appetite. Last but not least, hot meals should always be prepared with care, served warm and eaten at a set table together with relatives or friends in a cosy atmosphere.

Several key benefit-value links in Fig. 28.3 were associated to the idiosyncratic characteristics of home-made meals. Dutch seniors stated that, although they remained fairly good eaters, they did not have as much appetite as in past years. Therefore, meals that looked and tasted good were essential to stimulate eating and guarantee an adequate food intake. Good appearance and good taste (like potatoes that remained in one piece and crunchy vegetables) were in turn believed to be the result of the simplicity, diversity and freshness of home-made meals, which were thus seen as paramount in leading a healthy diet.

Similarly important to a healthy and safe diet was the amount of control provided by preparing one's own meals over what and how much food was bought, cooked and eaten daily. Moderation was the key word, not the least to avoid overweight and overspending. Cooked dinners reportedly contained only a small portion of red meat, which was sometimes replaced by poultry, fish or a vegetarian entrée. Cooking fat and processed fruits and vegetables were also avoided, as high amounts of saturated fat, food additives and salt were believed to be health-damaging. This negative association between industrial processing and a healthy diet was observed in earlier studies with ageing consumers (Fjellström *et al*, 2001; Hielkema and Kuyer, 1995; Oakes, 2003), as well as the link between the consumption of highly processed foods and lower socio-economic status (Horwarth, 1993).

Clearly, the preparation and consumption of home-made meals was seen by Dutch seniors mostly as a source of joy and pleasure, both on its own right and as a catalyst for togetherness. But it was likewise clear that they mostly saw meal preparation as a (housewife's) duty: regardless of whether one had time and energy to cook, or actually enjoyed it, dinner should be prepared from scratch every day. Moreover, people who were not willing to cook regularly or searched for alternatives to cooking were considered lazy. Remaining active and independent was given a high self-esteem value by target consumers. Self-esteem also played an important role in compelling senior women to put great care, effort and creativity into meal preparation, as this earned them a great deal of approval from relatives and social acquaintances. The notion of the proper dinner being that cooked by the housewife and shared with the family thus remains a strongly held social norm by older Europeans (Herne, 1995; Mäkelä, 2000; Marshall, 2000; Murcott, 1995).

Table 28.2 depicts the strength of target consumers' associations between attitudes towards and the frequency of several meal preparation behaviours. The frequency with which seniors reportedly prepared their own hot meals was strongly associated with their viewing of this activity as a daily habit or chore. A high involvement with food, a low convenience-orientation (Candel, 2001) and a high enjoyment of cooking also increased the frequency of meal preparation, as well as of trying out new recipes. Conversely, the same attitudes displayed

Table 28.2 Significance and strength of target consumers' ($n = 112$, 55–85 years old) associations between self-reported attitudes towards meal preparation and the frequency of several meal preparation and consumption behaviours (two-tailed Spearman's rho: [a] significant at the 0.01 level, [b] significant at the 0.05 level)

	Cooking	Trying new recipes	Convenience foods' use	Ready meals	Takeout	Eat out	Cold meal	Warm-up leftover	Skip dinner
Involvement with food	0.21[b]	0.25[b]	−0.01	−0.09	−0.12	0.08	−0.13	−0.24[b]	−0.34[a]
Enjoyment of cooking	0.22[b]	0.44[a]	−0.21[b]	−0.18	−0.08	−0.08	−0.25[a]	−0.02	−0.35[a]
Convenience-orientation in cooking	−0.36[a]	−0.30[b]	0.23[b]	0.29[a]	0.17	0.20[b]	0.30[a]	0.15	0.27[a]
Cooking as a habit	0.47[a]	0.13	−0.34[a]	−0.40[a]	−0.41[a]	−0.41[a]	−0.21[b]	0.00	−0.27[a]
Cooking as a duty	0.35[a]	−0.04	−0.21[b]	−0.27[a]	−0.34[a]	−0.35[b]	−0.16	−0.20[b]	−0.19
Being expected to cook	0.31[a]	0.04	0.03	−0.21	−0.22	−0.18	−0.10	−0.13	−0.21
Being appreciated for cooking	0.14	0.15	−0.20	−0.15	−0.00	−0.09	−0.05	−0.12	−0.14
Being the family's care-giver	0.20	0.30[a]	−0.06	−0.24[b]	−0.17	−0.02	−0.08	0.17	−0.31[a]

negative associations with the reported frequency of usage of convenience foods and HMR. This was particularly the case for viewing cooking as a habit or a duty, and for a low convenience-orientation. Other studies have also pointed out to the high self-relevance of cooking and the consequent low moral status of convenience in food preparation, especially among older female meal preparers (Gofton, 1995; Goldsmith *et al.*, 1995; Haire, 1950; Herne, 1995; Milburn, 1995; Thompson, 1996).

Target consumers' evaluation of ready meals

The high personal relevance attached to the preparation of home-made meals, and the resulting negative evaluation of the convenience features of ready meals, seemed to influence the actual target market's demand for the latter only to some extent. Half of the seniors participating in the qualitative study declared to be regular users (at least once a week) of ready meals, with 34% of all Dutch ready meal consumers being older than 55 years (Costa *et al.*, 2001b). Knowledge about the ready meals on offer was equally very good; even non-regular users knew a wide variety of products and could accurately describe many of them. That the consumption of such products is far from being restricted to young and busy singles or dual-income couples with no children, who do not care much for cooking and eating – a stereotype overly reinforced by many marketing and public opinion campaigns – has also been confirmed by several other European studies on the dietary habits of the ageing (Hautvast *et al.*, 1992; Schlettwein-Gsell *et al.*, 1991).

Figure 28.4 depicts the target market's hierarchical value map for the consumption of ready meals on weekdays. As can be readily observed, Dutch seniors reportedly have strong motives both for and against the consumption of ready meals. Their level of convenience in acquisition and storage was a highly appreciated feature, with participants naming a few situations where these products would come in handy – when having unexpected guests for dinner, during holidays or when one just came back from them and had no fresh food in store, and when prevented from shopping or cooking due to sudden illness. Another prized feature was the ample assortment on offer. Besides ensuring a varied diet, prepared meals were considered quite handy when wanting to eat a highly liked dish that was too difficult to prepare at home.

Yet another reported advantage of ready meals was their level of readiness for consumption, though only in situations in which the benefits achieved by not cooking conferred to the use of these products the necessary degree of appropriateness. Such benefits were, for instance, having more time to be socially active and more stamina to remain self-standing and enjoy other niceties of daily life besides eating. But not surprisingly, the high level of readiness for consumption of ready meals also rendered them quite unsuitable in the eyes of the large majority of target consumers. These products were only seen to suit those who could not or would not make the necessary effort and time available to cook and enjoy a good meal in the company of their family (e.g., 'the really old and sick', 'widowers', 'young people today', 'working families'). And

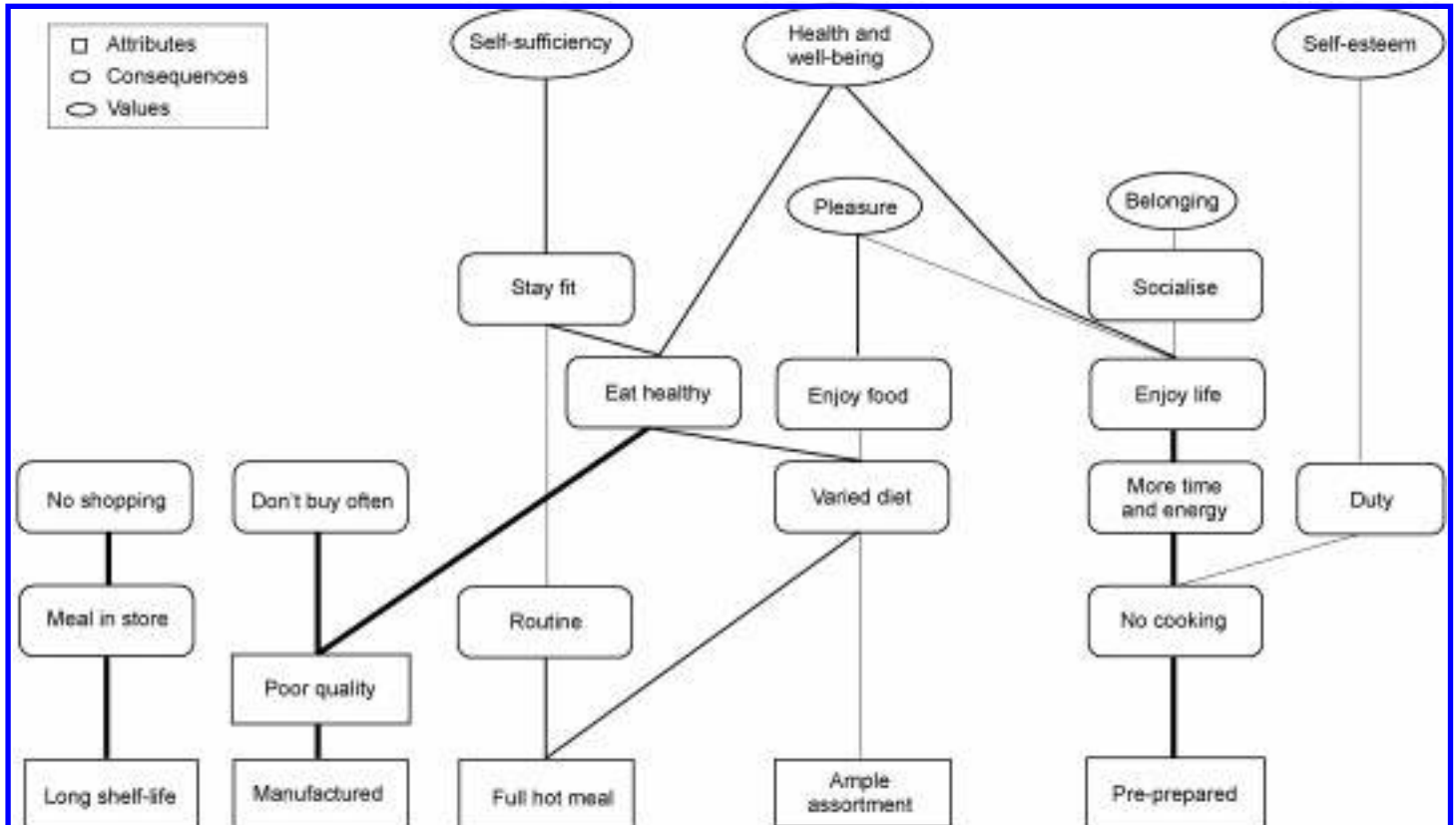

Fig. 28.4 Seniors' (55–87 years old) hierarchical value map of the consumption of ready meals on weekdays ($n = 25$). The thickness of the connecting lines indicates the strength of the associations between the cognitive elements.

although the former were hardly the subject of reproach, the later were seen as sadly neglecting their duties towards themselves and others.

The target consumers' perception of ready meals being mainly standardised, mass-produced, unappetising and unwholesome foods was the last strong motive supplied against their regular consumption. These products were judged to be prone to quick spoilage and contain poor quality ingredients (e.g., overcooked vegetables) as well as excessive amounts of salt, fat and food additives. Such an overwhelmingly negative appreciation of the quality of ready meals derived mainly of them being seen as the outcome of manufacturing rather than household processing. Nevertheless, Dutch seniors generally conceded that these products, though by far not as tasty and satiating as the result of their own cooking, were still full hot meals and thus preferable to cold meals, snacking or grazing. The role of daily hot meals in preserving important eating and living routines of ageing households has been equally highlighted in other studies (Herne, 1995; Sobal, 2000).

Table 28.3 shows the strength of target consumers' associations between attitudes towards ready meals and the frequency of several meal preparation behaviours. The frequency with which seniors reportedly used ready meals was significantly associated with a positive evaluation of their healthiness and tastiness, the appropriateness of their convenience in preparation and the extent to which they lend themselves to be part of a shared meal. This positive evaluation was also strongly related to a higher consumption of convenience foods and, to a lesser extent, of takeout and restaurant meals. Finally, it was interesting to notice that while a positive overall attitude towards the consumption of ready meals was not necessarily associated with a higher likelihood of replacing homemade meals with cold meals, warmed-up leftovers or skipping dinner altogether, viewing cooking as a habit or a duty, a high involvement with food, a low convenience-orientation and a high enjoyment of cooking all seemed to lessen the frequency with which such behaviours took place. These findings are amply supported by other similar studies (De Boer *et al.*, 2004; Hielkema and Kuyer, 1995; Oude Ophuis *et al.*, 1994; Sobal, 2000).

During the opportunity definition phase, target consumers also evaluated specific meal replacement products (frozen pizza, canned meal soups, dried Italian-style pasta, chilled hotpot and differently processed versions of Oriental-style noodles), their attributes and the benefits delivered (Costa *et al.*, 2002; 2007). Although all these products were among those regularly consumed by the target market (*Costa et al.*, 2001b), only the frozen pizza appeared to present them with an acceptable trade-off between convenience in preparation on one hand and healthiness and tastiness on the other. The perceived simplicity of most frozen pizzas gave seniors the opportunity to add extra toppings of their own choice and enough reason to prepare a green salad on the side. Not only was adding more ingredients and preparing side-dishes seen to improve considerably the sensory and nutritional quality of the product, but also, and most importantly, it provided seniors with a welcomed opportunity to feel more involved in the preparation of their own meal. All of the remaining products

Table 28.3 Significance and strength of target consumers' ($n = 112$, 55–85 years old) associations between self-reported attitudes towards ready meals and the frequency of several meal preparation and consumption behaviours (two-tailed Spearman's rho: [a] significant at the 0.01 level, [b] significant at the 0.05 level).

	Cooking	Trying new recipes	Convenience foods' use	Ready meals	Takeout	Eat out	Cold meal	Warm-up leftover	Skip dinner
Appropriateness of ready meals' convenience in preparation	−0.17	−0.11	0.22[b]	0.21[b]	0.19	0.22[b]	0.04	−0.14	−0.07
Healthiness of ready meals	−0.14	−0.12	0.22[b]	0.22[b]	0.05	0.18	−0.03	0.23[b]	0.02
Tastiness of ready meals	−0.05	−0.10	0.32[a]	0.19	0.14	0.14	0.09	0.10	0.03
Fittingness in a shared meal	−0.08	−0.14	0.36[a]	0.28[a]	0.33[a]	0.17	0.16	0.11	0.05

were mostly viewed by target consumers as unhealthy, unappealing, expensive and not really simpler or quicker to prepare than the home-made versions. This was a somewhat surprising outcome given previous assumptions about seniors' relatively higher preference for products that closely mimic traditional home-made meals (Herne, 1995; Laureati *et al.*, 2006; Sonneveldt, 1996). In view of this it might be wise not to overestimate the importance of tradition as a determinant of seniors' choice of meal solutions.

The other problematic trade-off represented by ready meals was that between storage convenience and freshness. Some seniors found no ready meal ever to be fresh, since they were all pre-processed. Others found chilled meals to be the most fresh, because they had been packed under cooling right after their preparation and had a short shelf-life. Others yet found frozen meals to be the most fresh and convenient because they had a long shelf-life and their ingredients were 'fresh frozen'. Finally, dried and canned meals were highly appreciated because of their storage convenience, but unanimously considered not fresh.

Opportunities for development of new ready meals

The NPD process, as it is depicted in Fig. 28.1, might lead to the conclusion that a consumer-led approach to food innovation is necessarily one of a highly sequential nature and narrow focus, i.e., a linear, end-to-end search for one product that matches the needs of one target market. However, the everyday practices of R&D and marketing departments, as well as those of the several other company functions involved in the development and launch of new food products, are far messier. Sometimes they are concurrent and iterative, or partially overlap, to guarantee the efficiency and effectiveness of the process; often enough, though, and to the misfortune of many innovation efforts, they can become downright redundant and even antagonistic (Dahan and Hauser, 2002b; Fuller, 2004; Griffin and Hauser, 1996).

NPD should always start with a broad range of ideas from as many sources as possible, which will later be winnowed down to a few high-potential product concepts. Only some of these, in turn, will finally be developed and launched. It is often much cheaper and more effective to test many alternative concepts at an early stage than to modify an unsuitable product at pre-launch or introduction, or to have a market flop. Ideally, consumer-led food product development should support the creation of new product platforms for pre-specified market environments, given that the existence of main common elements enables mass-customisation and more effective development processes (Dahan and Hauser, 2002b).

Taking into account all the information collected from the target market during the strategic assessment and the opportunity definition phases, there clearly seemed to be two main areas where meeting seniors needs through the development of innovative technology and new ready meal platforms could be potentially profitable. One was to address the trade-off between the appropriate level of convenience in preparation on one hand, and healthiness and tastiness

on the other. This could be achieved by developing meal replacements the preparation of which would require just the right amount of extra ingredients and own cooking. The other would be to develop the necessary processing technologies for such products to be composed of raw or minimally processed ingredients (addressing target seniors' demand for both freshness and suitable levels of convenience in preparation), and yet have a reasonably long shelf-life. In view of this, the development opportunities uncovered were:

- The manufacture of chilled, ready-to-eat meal components for the retail market (but not necessarily pre-packed), so that seniors could 'mix and match' their dinners to resemble the highly popular orders from Oriental take-out outlets.
- The manufacture of ready meals tailored to the needs of ageing consumers following special diets (institutionalised or not), whether due to a particular health condition or just the wish to prevent certain types of illnesses and promote a better overall health status.

Opportunity refinement

At this stage, a comprehensive analysis of the relationships between the attributes linked to consumption benefits deemed relevant by the target market and the main technical features to be displayed by new products takes place. The goals of such an analysis are to give shape to products that fulfil the target consumers' needs in a unique and superior way, as well as developing marketing strategies that communicate the successful fulfilment of needs. Therefore, this is perhaps the most crucial moment in a consumer-led food product development process in guaranteeing that value to both consumers and producers is created (Costa and Jongen, 2006; Urban and Hauser, 1993; van Trijp and Steenkamp, 1998).

The research project described in the previous sub-section, which studied the motives underlying Dutch seniors' choice of meal solutions and their relative importance, uncovered three main dimensions that could constitute rewarding development opportunities for ready meals. These were:

1. easy to prepare, but allowing a certain degree of participation in the making of the final product;
2. freshly prepared from raw ingredients, but with a reasonably long shelf-life;
3. familiar, but not necessarily traditional.

With the aim of verifying whether these three main themes could constitute potentially rewarding new product platforms, five product concepts were created to be evaluated by target consumers, the description of which in shown in Table 28.4 (Costa, 2008b). These concepts were thought to constitute both potential optimum equilibrium points within one or more of the dimensions structuring the demand and technologically feasible development opportunities.

Fifty-seven Dutch female meal preparers (55–84 years old, 75% retired, 45% living in single-person households, 80% regular users of ready meals, 70% with

Table 28.4 Ready meal concepts submitted to the target consumers' evaluation (Costa, 2008b). [a] Resembled products existing in the market at the time but unknown to target consumers; [b] Resembled a product recently introduced to the market; [c] Did not resemble any of the products existing in the market at the time

	Main ingredients	Preservation method	Shelf-life	Preparation instructions
Paella[a]	Seafood, chicken, peas, red peppers, onions and rice	Minimally processed, mixed and frozen	One and half years	Heat oil in a pan. Add the contents of the package and fry for 15 minutes
Tuna salad[a]	Tuna, potatoes, green peppers and maize	Mixed, sterilised and canned	Two years	No preparation required
Hotpot kit[c]	Meatball, potatoes, carrots and onions	Minimally processed, packed under controlled atmosphere in separate containers and chilled	Five days	Cook the potatoes, carrots and onions in boiling water. Mash and season to taste. Fry the meatball and prepare the gravy according to your own recipe
Steam[b] salmon	Salmon, small potatoes and green beans	Minimally processed, packed together under controlled atmosphere and chilled	Five days	Heat in the microwave for 2–4 minutes without opening the package. Cooks in its own steam until pressure is released through the valve
Pizza kit[c]	Pizza dough, tomato sauce, ham and grated cheese	Minimally processed, packed under controlled atmosphere in separate containers and chilled	Twelve days	Spread the pizza dough with a roll and cover with the tomato sauce from the plastic bag. Add the ham and any other of your favourite toppings, and season to taste. Cover with the grated cheese and bake in the oven until ready

a high level of category knowledge) were asked to classify 59 HMR according to their written descriptions, including the five product concepts and 54 other products frequently consumed at the time (Costa *et al.*, 2001b), in a choice-oriented, free sorting task (Michela and Contento, 1984; Steenkamp *et al.*, 1994; van Kleef *et al.*, 2005). They were also asked to provide labels for the groups of sorted products as well as the criteria underlying the classification process. These labels and criteria were content-analysed and the frequency with which each criterion was used by respondents determined.

Eight classificatory criteria were used by more than 75% of target consumers: convenience, familiarity, freshness, healthiness, seasonality, taste preference, type of protein and type of staple. As described in the previous sub-section, all of these criteria constituted important dimensions underlying the target consumers' choice of ready meals, with the possible exception of seasonality, type of protein and type of staple. The latter could be associated with a tendency to favour products seen to guarantee a varied diet – a key benefit for the target market – thereby constituting a valid preference dimension (Rappoport *et al.*, 1992). However, they could also have been used as perceptual dimensions by participants, i.e., as means to establish comparisons between products based merely on their degree of similarity (Axelson *et al.*, 1986; Moteleone *et al.*, 1997). If that was the case, the last three dimensions may not be necessarily relevant to the target market's product choice (Creusen and Schoormans, 1997).

In a second stage, a matrix containing the frequencies with which target consumers classified the product concepts according to the eight classificatory criteria was generated and submitted to a correspondence analysis (Greenacre, 1994; Snelders and Stokmans, 1994). Figure 28.5 shows the results of this analysis and indicates that the criteria differentiated well among each other and between the product concepts. The hotpot kit was perceived by target consumers mainly as a familiar product, typical from wintertime. This meal solution was sometimes also classified as fresh, because it was made out of chilled, minimally processed ingredients, but almost never as healthy or tasty given that it did not contain any green vegetables. Moreover, it was often seen as inconvenient since it displayed a relatively short shelf-life and was perceived to require approximately the same level of preparation as its home-made counterpart.

Conversely, the steam salmon dish and the frozen paella were essentially characterised by their main components and their perceived freshness, while the pizza kit and the tuna salad were more frequently seen as tasty and appealing meal solutions. The later result is in agreement with the findings described in the previous sub-section, which indicated a high preference of the target market for pizza products, on one hand, and for ready-to-eat meal solutions with a very long shelf-life on another. Nevertheless, both the pizza kit and the frozen paella were more often seen as unhealthy and inconvenient meals than the steam salmon dish and the canned tuna. This was mainly because the former were judged to contain fewer green vegetables and to be relatively more complex and slow to prepare than the latter (though clearly not as much as their home-made counterparts). In another study, North-American women aged 64 years and

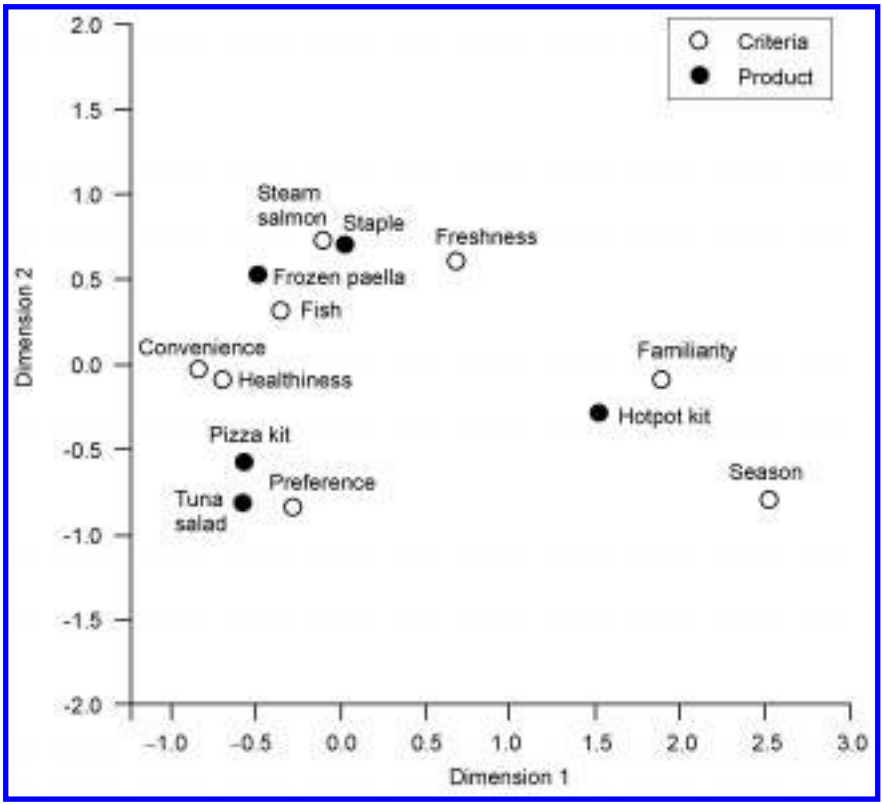

Fig. 28.5 Correspondence analysis map resulting from seniors' (55–84 years old) categorisation of five ready meal concepts according to eight sorting criteria ($n = 57$).

older have equally indicated to perceive canned tuna as a fairly healthy food (Oakes, 2003). The steam salmon was also more frequently classified as fresh than the paella, highlighting that chilled meal solutions were more readily perceived by target consumers as fresh than their frozen counterparts. Finally, the tuna salad, being canned, was almost never perceived as fresh, while the steam salmon was often seen as an unappealing meal solution because of its relatively short shelf-life.

It is interesting to notice that the chilled hotpot kit – a concept based on a fairly innovative technological concept that did not resemble any of the ready meals existing in the market at the time – was classified as familiar because it closely mimicked a traditional Dutch recipe. This seems to indicate that one of consumers' strategies to create representations for new products is to use information contained in pre-existing product categories, thereby avoiding the creation of new knowledge structures and/or major restructuring of existing ones (Moreau *et al.*, 2001). Such a cognitive strategy might facilitate the acceptability of truly new products (Stayman *et al.*, 1992; Sujam and Bettman, 1989) and novel foods (Tuorila *et al.*, 1994), and could consequently be employed in the

development of innovative meal solutions and respective marketing strategy. However, the hotpot kit was not often seen as an appealing concept, since it was not perceived to be really simpler or quicker to prepare than its home-made version or to offer any welcome chance of flavour variation. Meanwhile, the chilled pizza kit received a positive evaluation from target consumers because, although fairly innovative and relatively complicated to prepare, it represented a well-known product with an enhanced feature that was highly appreciated – the possibility of one adding toppings of choice. Taken together, these findings support the conclusion earlier drawn that familiarity alone, without any other added value, may not be enough to guarantee a successful meal solution for this target market.

The outcome of the classification task performed by Dutch seniors provides a good overview of how these target consumers perceived product concepts and their underlying technological processes to match desirable attributes of ready meals and associated benefits. Importantly, it also provides valuable guidance for the creation and communication of the market positioning of potential new products (Cohen and Basu, 1987). Finally, it showed that the ready meal concepts tested, though for their large majority fairly new and supported in innovative technologies, were only moderately incongruent with the product-category schemes held by target respondents. This could play a role in facilitating their acceptance (Stayman *et al.*, 1992; Sujam and Bettman, 1989). Nevertheless, the classification task outcome equally showed that congruency and familiarity should not be enhanced, either in new food products or associated marketing strategies, at the expense of other features providing key benefits to senior consumers.

28.4 Conclusions and future trends

This chapter has demonstrated how the design of new foods and beverages for an ageing population can be addressed by a consumer-led approach to product development. Moreover, the methodology described has also provided useful findings regarding (1) how seniors go about choosing their meals and ultimately their food, and (2) how their wants and needs regarding meal choice can be addressed in a way that adds more value to both them and the food industry in general.

Future trends in technological development will most likely continue to focus on the sensory and nutritional needs of the ageing. More effective and wholesome strategies will have to be devised to compensate for age-related impairments in odour, flavour, trigeminal mouth feel and texture perception. These will open the door for important developments in the food ingredients' industry. Similarly, the perspective of being able to prevent the onset or worsening of many ailments affecting the ageing – heart disease, osteoporosis, diabetes, kidney disease and certain types of cancer – through an adequate intake of essential nutrients and dietary fibre will continue to drive the exponential

growth of R&D efforts in the area of functional foods and dietary supplements (Fillion and Kilcast, 2001; Herne, 1995; O'Donnell, 1994; Roberts, 2002; Rolls, 1993; Russel *et al.*, 1999; Wysocki and Pelchat, 1993).

There are often many remarks made by seniors about the packaging and labelling of foods. Portion sizes are seen as excessive for single or two-person households and packages as too big, too difficult to handle and creating too much waste. Most related complaints also stress the need for easy-to-open packages that keep components separate and allow buyers to see the food inside. Labels, on the other hand, are generally thought be vague and not informative enough, besides being written in impossibly small fonts. These are all well-known aspects of concern in regards to the packaging of manufactured products targeted at the ageing that, for the most part, still wait to be properly addressed by the food industry (Fillion and Kilcast, 2001; Roberts, 2002).

The consumption of plenty of fluids (water or any non-alcoholic, caffeine-free, low on sugar equivalent) is increasingly recommended for older individuals (Russel *et al*., 1999). Ageing people can suffer from a reduced thirst mechanism (Rolls and Phillips, 1990; Stout *et al.*, 1999), and must make a conscious effort to drink more and keep well-hydrated, particularly in this era of global warming. Therefore, the current bloom of the mineral water, natural fruit juices and herbal tea industries will be more and more sustained by the need of the many ageing to quench their thirst in a healthy but pleasant manner.

Seniors' meal and food choice differ little from everybody else's: a constant struggle between equally strong desires for taste and health, convenience and autonomy, routine and variation, the safety of the familiar and the allure of the new. The only significant difference is that to keep on winning that struggle everyday is harder and more vital for them than for most other people. The food industry, as everybody else involved in better feeding the ageing, should have the ability and the willingness to alleviate that for them. Not least because in less than twenty years, one out of ten people in the world will be older than sixty (WHO, 1991), and the most fortunate of us will, sooner or later, be one of them.

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