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### Nutrition and Bone Health in Old Age

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#### 1. Introduction

Osteoporosis is a progressive skeletal disease characterized by loss of bone mass and density. It is the second leading healthcare problem in the world after cardiovascular diseases, according to the World Health Organisation. The prevalence of osteoporosis is increasing due to progressive aging of the population.

Bone mass loss from both the spine and hip, starting at the post-menopause in women and around 60 years of age in men, continues during aging. It is also at old age when the vast majority of fractures due to bone fragility occur and when measures intended to minimize such losses, including the diet and other aspects related to nutritional status, are therefore particularly important.

The role of nutritional deficiency in the production of bone growth changes and promotion of osteoporosis in the elderly is well known today. Multiple factors are involved in bone mass loss in these stages of life, including decreased bone formation, decreased calcium absorption by the intestine, changes in regulation by calciotropic hormones, physical activity, nutritional status, and so on.

While calcium has been shown to have a beneficial effect on bone health at all ages, individual nutritional intake of calcium is below the recommended levels in all countries and at all ages. The best way to achieve an adequate calcium intake is through a balanced diet that should include dairy products.

Vitamin D deficiency is common in many elderly populations and increases fracture risk. Regular exposure to sunlight, taking vitamin D-rich food and vitamin D supplements when required, helps maintain adequate levels of the vitamin.

Bone is a live and active tissue that is continuously being remodeled by the formation of new tissue and elimination of old tissue. This remodeling may be affected by nutritional deficiencies and dietary excesses. This article analyzes how main food items in our diet could influence bone formation and health.

#### 2. Aging and bone mass. The role of nutrition

#### 2.1 Importance of bone mass

Bone mass is clearly the most significant factor related to fracture pathogenesis. Experimental studies have found a high *in vitro* correlation between bone resistance to fracture and bone mineral density (BMD) in both the lumbar spine and femoral neck. Bone mass has been reported to have a different relative importance in fracture incidence depending on the type of bone and bone structure. The contribution of bone mass to femoral neck fracture represented 85% of all factors, while in other bones the relative importance ranged from 67% and 82% (1).

#### 2.2 Changes in bone mass over time

Bone mass at any age is the result of two variables: the amount of bone accumulated during growth, known as peak bone mass, and the subsequent proportion of bone lost.

In humans, bone density increases during the growth period and continues to increase even after growth, when height stays constant, reaching a peak at 25-30 years of age for bone with a mainly trabecular composition (vertebra) and at 35-40 years of age for bones with a mainly cortical composition (femur and radius). It is estimated that 90% of bone mass accumulates up to 20 years of age, and an additional 10% between age 20 and 35 (2). It is obvious that an inadequate accumulation of skeletal mass during youth increases the risk for a fracture incidence at subsequent stages of life (3).

Age is the most important determinant in BMD, and it is known that an overall decrease in the amount of cortical bone, and more specifically of trabecular bone, occurs from a certain age, leading to the so-called age-related physiological osteopenia (4,5). This decrease, measured using densitometric techniques, has been estimated to start from approximately 40 years of age, and cumulative losses at 80-90 years of age are 30% in men and 45%-50% in women. This loss is not linear and is more significant in the early post-menopausal years in women, after which an overall annual decrease by 0.5%-1% occurs. The loss affects trabecular bone and, less markedly, cortical bone (6,7).

In women, the significance of the relationship of bone mass loss to estrogen deficiency is well known (8). It is also known that while in elderly men bone mass has no relationship to androgen levels, a close relationship exists in women between BMD and estrogen levels. It is therefore concluded that estrogens may play a significant role in the maintenance of skeletal mass, at least in the elderly (9,10). Moreover, BMD improvements have been seen in patients, both men and women over 70 years of age, treated with low androgen doses (11). Table 1 summarizes all other factors.

#### 2.3 Pathophysiology of bone mass loss in the elderly

Multiple factors are involved in bone mass loss, including decreased bone formation, decreased calcium absorption by the small intestine, changes in the regulation of calciotropic hormones, physical activity, overall nutritional status, and so on. Each of these factors are discussed in more detail below.

- 1. Decreased osteoblast function
- 2. Decreased intestinal calcium absorption
- 3. Changes in calciotropic hormones
- 4. Other factors

Table 1. Aging and bone mass loss. Most common causes for bone mass loss.

#### 2.3.1 Decreased osteoblast formation

A decreased bone formation occurs with increasing age, partly related to overall osteoblast aging. However, the fact that these cells are able to respond to adequate stimuli, as occurring in fractures in the elderly, where callus develops, suggests that the mechanism actually subsiding is the lack of action of local factors which are mediators in this action, such as insulin-like growth factor-1 (IGF-1), also called somatomedin C (12).

It is known that with age a decrease occurs in the endogenous function of the growth hormone-releasing hormone (GHRH) that contributes to reduced growth hormone (GH) secretion (13). The formation stage of the remodeling cycle would also be decreased. This stage, which normally lasts 80 days at 40 years of age, is reduced to 60 days in subjects older than 60 years. (14)

#### 2.3.2 Decreased intestinal calcium absorption

Decreased calcium absorption with age may contribute to the development of osteopenia. This has been shown with techniques that measure intestinal calcium absorption using isotopically labeled calcium, and could be related to either a vitamin D deficiency that may lead to osteomalacia when this deficiency is very pronounced or to a decreased conversion of vitamin D into 1,25(OH)<sub>2</sub> vitamin- D in the kidney. It is known that overall kidney function is physiologically impaired with age, and renal synthesis of this hormone is therefore decreased. Finally, some authors suggest that intestinal vitamin D receptors decline with age, which causes a relative resistance to calcitriol and a resulting impairment in intestinal calcium absorption (15).

The demonstrated therapeutic effects of vitamin D administration for fracture prevention (16) are in line with this hypothesis. Several studies conducted in both men and women reported that low vitamin D levels in the elderly were related to both estrogen deficiency in women and low androgen levels in men (17). Thus, at advanced ages, calcium and vitamin D supplements given to women with a low calcium intake and vitamin D deficiency had a significant effect on bone mineral density, with increases by  $0.5\pm4.8\%$  (p=0.02) in the hip and  $2.12\pm4.06\%$  (p=0.04) in the lumbar spine (18,19,20, 21).

#### 2.3.3 Changes in calciotropic hormones

There may also be hormonal factors related to age-related osteopenia. Vitamin D is a steroid prohormone that is obtained either by photosynthesis in the plant, through its conversion in the human skin, or through nutritional intake. As already discussed, a great number of

changes in vitamin D metabolism have been reported in the elderly. Exposure to sunlight typically decreases with age because of limitations of elderly people to walk, due to institutionalization, etc. However, a decrease also occurs in the capacity of the skin conversion of the vitamin (22). In addition, a decrease occurs in renal production of calcitriol that is attributed to aging itself. While parathormone (PTH) levels increase with age, PTH is not able to increase the synthesis of 1,25(OH)<sub>2</sub>vitD (23). Higher PTH levels would cause an increased bone resorption and, thus, osteopenia.

Calcitonin (CT) levels, both basal and in response to calcium infusion, have also been shown to gradually decrease in elderly subjects of both sexes. This is due to either a decrease in the functional capacity of thyroid C cells or a decreased capacity of such cells to respond to natural secretagogues, such as calcium or pentagastrin.(24)

#### 2.3.4 Decreased physical activity

Aging leads to a decrease in physical activity. As this is a significant factor in bone formation, a decreased physical activity would involve a reduced bone formation in elderly subjects (25).

#### 2.3.5 Nutritional changes

There are various nutritional changes in the elderly that may contribute to bone mass reduction. A deficient calcium intake at this age has been shown, due to either a decreased dietary supply or gastrointestinal problems related to aging (26). Wasting diseases, eating alone, taste loss, swallowing problems, unmet special dietary requirements, and even economical factors are factors contributing to the weight loss and malnutrition occurring in elderly people, leading to a decreased calcium intake. Elderly people with chronic diseases with or without disability and those with acute conditions have considerable changes in markers of nutritional status.

The reduced calcium intake, is a risk for increased negative calcium balance which is attempted to be balanced by an increased calcium passage from bone stores to plasma, causing bone demineralization, albeit to some extent, calcium homoeostasis can be achieved by increased tubular re-absorption.

Structured questionnaires to assess nutritional risk are now available, including Mininutritional assessment (MNA) and its short form, MNA-SF (27,28).

#### 3. Special nutritional needs in the elderly: Energy, protein, minerals, vitamins

#### 3.1 Energy

At this stage of life, an adequate, balanced diet that allows elderly subjects for duly carrying out their daily activities and for maintaining a satisfactory state of health is very important. However, studies suggest that nutritional and energy deficits frequently exist in the elderly (29,30).

The limitations of basal energy expenditure and expenditure caused by thermogenesis provide a first guideline for assessing energy intake in elderly people. (31) A decrease in intake by up to 600 calories between 30 and 80 years of age has been reported. Loss of

physical activity alone would account for a reduction of virtually 400 calories. In the Baltimore longitudinal study in elderly subjects, requirements decreased from 2,700 cal/day at 30 years to 2,100 cal/day at 80 years.

In the NHANES study, men in the 24-34 year age group had an intake of 2,700 cal/day. From 65 years of age, mean intake was 1,829 cal/day. In women, the same age groups showed a reduction from 1,800 cal/day to 1,259 cal/day (32).

The RDAs are 2,300 cal/day for men weighing 65 kg and 1,900 cal/day for women of the same weight, both over 51 years of age. In both cases, intake is approximately 30 cal/kg body weight/day (33). Energy reduction may involve the loss of essential nutrients. Iron, thiamine, riboflavin, niacin, vit. A, vit. C, and calcium deficiencies are most common. The decreased efficiency by which the elderly absorb essential nutrient some factors such as iron and vitamin C should also be considered.(34)

#### 3.2 Protein

Protein requirements in healthy elderly subjects are highly controversial, not only with respect to the amount of protein, but also the amount of required individual amino acids, especially for the essential amino acids.

The nutritional recommendation is to provide the same amount of proteins as for young adults, approximately 20% of energy intake, but since muscle mass is decreased, with this protein recommendation the amount of protein per kg of lean fraction is higher. This recommended intake is not intended to increase muscle mass, but rather to provide an amount of protein sufficient to avoid a deficient intake.

Protein supply is related to energy supply. The recommended dietary allowance (RDA) of protein is 0.8 g/kg/day. This may be adequate when the diet provides adequate energy. However, when the limits are at 30 cal/kg body weight/day, this RDA may be low for achieving positive nitrogen balances, as in the case of low energy consumption, amino acids could be converted into glucose and keto-bodies for energy delivery, and are therefore lost for more specific functions. It has therefore been suggested that such an amount may be inadequate for maintaining nitrogen balance in healthy, ambulatory elderly subjects because the efficacy with which elderly people use these proteins may be decreased during the aging process. An intake of 1 to 1.25 g/kg/day, adequately meeting the requirements in healthy elderly people, is thus recommended (35). This amount should be even further increased under conditions of disease, stress, or lesion to prevent malnutrition. The heterogeneity of the elderly population should however be considered, and these recommendations should be adapted to each individual and situation. Protein requirements should be increased (up to 1.5 g/kg/day) in people under stress conditions such as infection, fracture, surgery and specially healing of bedsores, and are reduced in renal and/or liver insufficiency.

Protein should represent at least 12% of the diet's calories, and two thirds of the amount provided should be in the form of proteins of animal origin with a high biological value. Higher intakes are not recommended because they do not slow muscle catabolism and may impose an excess overload on the liver and kidney (36). Protein deficiencies in elderly people are not rare. Signs of protein deficiency include fatigue, delayed healing, and decreased physical resistance (30,37).

Proteins of a high biological value, i.e. rich in essential amino acids, should be taken. Milk, cheese, and eggs may therefore be preferred to meat, meat products, fish, etc. because the former are easier to obtain, store, and prepare.

#### 3.3 Lipids

Approximately 30% of total calories should be provided by fat. Absorption of lipid-soluble vitamins is very much reduced without fat. It has not been clearly elucidated to what extent fat intake should be restricted in the elderly, as severe restrictions could affect several of their functions and may also cause nutritional deficiencies. Low fat diets are unpalatable and usually poorly accepted by the population. These diets may enhance development of osteoporosis because of a decreased intestinal absorption and an increased renal loss of calcium and vitamin D.

Recent studies conducted in subjects over 65 years have noted that a high intake of polyunsaturated fat is associated with an increased risk of osteoporotic fracture in the elderly, while a diet rich in monounsaturated fat decreases such risk. An inverse relationship was also seen between HDL cholesterol levels and risk of fracture (38).

#### 3.4 Calcium

Most calcium salts or compounds need hydrochloric acid for the conversion into soluble Ca<sup>2+</sup> and fractional absorption of calcium from the diet in general diminishes in patients with reduced gastric acid secretion. The importance of gastric secretion for calcium absorption takes on clinical relevance with aging. Hypochlorhydria, achlorhydria and atrophic gastritis all occur as a result of aging(39).

It is admitted that intestinal calcium absorption decreases by 30% to 50% in adult age (40). Approximately 99% of body calcium is in the skeleton; the remaining 1% is distributed among extracellular fluids and cell membranes.

On the other hand, age-related bone mass loss involves high risk of deformity, fracture, and disability. Variations in serum calcium levels (4.5-5.5 mmol/L) are maintained by the interaction of PTH, estrogens, CT, and vitamin D [ $1,25(OH)_2D$ ]. If calcium intake or absorption is inadequate, serum levels may be maintained at the expense of bone mineral. The recommended calcium (RDA ??) intake for men and women is 800 mg/day, and 1,500 mg/day for people over 65 years of age (41). The actual intake tends to be below those recommendations (42)

Milk and its products are the richest sources of calcium. Some people however avoid dairy products, do not take animal products, or do not tolerate lactose. Yogurt may be a good source of calcium for people who do not tolerate lactose because the bacterial cultures used for yogurt production contain some lactase and this fact promotes its digestion. It is known that with lactose, efficacy in calcium absorption increases to 60% of intake; without lactose, absorption capacity decreases to 30%.(43). A way to receive adequate amounts of calcium while maintaining a low fat diet is to take partially or totally skimmed products, such as skimmed yogurt or milk or partially skimmed milk. Partially or completely skimmed milk contains almost the same amount of calcium as whole milk but much less fat.( usually, ca. 1.5%). Milk and dairy products however are not the only sources of calcium. There are foods

V	EGETABLES		
•	Cabbage	400	
•	Dry soya	226	
•	Swiss chard	110	
•	Pinto beans	106	
•	Lentils	79	
С	EREALS		
·	Enriched white bread	84	
N	UTS	$ )   \cap \langle ( -$	
•	Hazelnuts	250	
•	Dry almonds	234	
•	Walnuts	99	
•	Peanuts	74	
D	AIRY PRODUCTS		
•	Whole milk powder	909	
•	Pasteurized whole milk	123	
•	Skimmed milk	133	
•	Yogurt	150	
C	heese		
•	Emmentaler	1.180	
•	Edamer	900	
•	Cabrales	700	
•	Gruyère	700	
•	Roquefort	700	
•	Sheep cheese	400	
•	Cream cheese	300	
•	Burgos	210	
•	Camembert	162	
•	Cottage cheese	100	
F	ISH		
•	Sardines in oil (with spines)	354	
•	Sole	70	
	IEAT	8 to 12	
C	ONFECTIONERY		
	Molasses	273	
•	Milk chocolate	228	
[O	THER: Eggs (without shell)	40	

Table 2. Calcium content of some foods (mg/100 g)

with little fat but which are rich in calcium, such as oranges and cabbage. Calcium-enriched food may represent an alternative. When supplemental calcium is given, vitamin D should be administered concurrently to improve absorption. Supplements should preferably be given with meals and separate from treatments indicated for osteoporosis, such as bisphosphonates, because they may cause interference and the desired result is not achieved.

Certain characteristics of the diet may influence effective intestinal absorption of calcium. Protein-rich food contributes to create a slightly acidic urinary pH, which promotes calcium excretion in urine and contributes to bone demineralization. Fat, particularly saturated, decreases calcium absorption and enhances calcium excretion in urine (44). Fat intake should therefore be monitored. Phytic acid in whole meal flours and oxalic acid and uronic acid in vegetables may combine with calcium ions, forming salts and preventing their absorption. However, 50 g/day of fiber should be exceeded for these mechanisms to seriously compromise calcium supply (45).

Due to the above reasons, the National Osteoporosis Foundation (NOF) recommends a calcium intake of approximately 1,200 to 1,500 mg/day in elderly people. Higher intakes do not provide additional benefits and may increase the risk of renal stones or cardiovascular disease (46,47).

#### 3.5 Phosphorus

Phosphorus is essential for the structural integrity of the cell and for metabolic and catabolic reactions; it regulates a great number of enzymes and controls energy storage in the body, as well as energy transformations. Phosphorus plays a significant role in oxygen supply to tissues through 2,3- diphosphoglycerate and ATP levels in red blood cells. It is also part of the buffer systems in urine and plasma, and its presence may possibly be critical in the defense against infection (48). The body of a 70 kg adult contains ca.670 g of phosphorus, and the main sources of the mineral are milk and dairy products. Meat, fish, eggs, and cereals also provide phosphorus. The daily RDA for adults is 800 mg/day.

Excess dietary phosphate, associated with low calcium supply, causes hypocalcaemia, stimulation of PTH secretion, and bone mass loss. A dietary calcium:phosphorus ratio of 1 or higher and a maximum ?? total amount of phosphorus of 800 mg/day are therefore recommended. When this ratio is not met, even if the recommended calcium intake is met, demineralization may occur (49). Carbonated beverages (with gas) may contain high amounts of phosphorus, which alter bone remodeling. (50)

By contrast, except for diseases leading to hypophosphatemia, particularly renal and gastrointestinal and exceptionally congenital diseases, defect in phosphorus supply are rarely found in humans.

#### 3.6 Magnesium

This is an indispensable element required for biochemical processes affecting energy metabolism and neuromuscular transmission. It is also an essential cation in the control of calcium/phosphorus metabolism through the hormonal action of vitamin D, parathormone, and calcitonin (51). Magnesium absorption disorders and deficiencies related to advanced age do not apparently occur. Significant dietary sources of magnesium include nuts, cereals, legumes, bananas, vegetables, and dairy products, however, its intake is well distributed between the various sources.

Over fifty percent of the human body magnesium is found in bone. When magnesium deficiency occurs, the mineral is mobilized from bone, which may have an impact on bone health. As occurring with other minerals, the recommended daily requirements vary with

age and physiological needs. The recommended magnesium supply is 350 mg/day in adults and 300 mg/day in women (52).

Plasma magnesium homeostasis is achieved through changes in both intestinal absorption and renal excretion, more concrete renal re-absorption of the mineral. Only in cases of severe deficiency (lack of supply, malabsorption states, renal losses, etc.), magnesium is mobilized at the expense of its bone deposits together with increased magnesium absorption. This occurs through PTH and, to a lesser extent, vitamin D.

#### 3.7 Vitamins

The risk of restrictive diets is an inadequate micronutrient supply. The deficiency takes some time to manifest, but may have serious consequences. Table 3 provides some international recommendations for vitamin dietary intake.

Supply/day	Males	Females	
Thiamine	1.2 mg	1.0 mg (0.5 mg/1,000 kcal)	
Riboflavin	1.4 mg	1.2 mg	
Ascorbic acid	60 mg	60 mg	
Vitamin A *	1,000 mg	800 mg	
Vitamin D	700-800 IU	700-800 IU	
Vitamin K	80 ng	60 ng	
Niacin	15 mg	13 mg	
Folate	200 mg	180 mg	
Vitamin B <sub>6</sub>	2.0 mg	2.0 mg	
Vitamin B <sub>12</sub>	2.0 ng	2,0 ng	
Vitamina E	10 mg	8 mg	
(Tocopherol equivalent:	0.4 mg of Vit. E/1 g	polyunsaturated fatty acids)	
Biotin	30-100 ng	30-100 ng	

\*1 ng of retinol = 0.3 IU = equivalent to 6 ng of  $\beta$ -carotene in terms of vitamin A activity.

Table 3. RDAs (recommended dietary allowances) of micronutrients potentially related to reduced bone mass density.

It should be considered that some factors, such as smoking, emotional stress, high alcohol intake, drugs, etc. may strongly modify bioavailability and vitamin requirements in the elderly. Some gastrointestinal changes, such as atrophic gastritis, may lead to folate malabsorption due to pH changes in the proximal bowel. Intrinsic factors and vitamin  $B_{12}$  absorption are also affected by these changes (53). Homocysteine levels increase with age and are inversely related to levels of folates and vitamin  $B_{12}$ , two essential cofactors for remethylation to methionine. There are studies reporting a change in BMD related to vitamin  $B_{12}$  levels (54), and it has been suggested that folate supplementation may prevent fractures in elderly women, although it has not been shown to decrease bone metabolism. Lack of vitamin  $B_{12}$  has been proposed as an independent risk factor for osteoporosis and fractures (55,56).

Normal conversion of  $\beta$ -carotenes into vitamin A is usually decreased in the elderly, and it is therefore advisable to increase dietary intake of vegetables and fruit. Nevertheless, both

low and excess intake of vitamin A increases fracture risk. Independently, beta-carotene is by itself has been hypothesized to be associated with decreased risk of developing osteoporosis. Vitamin C helps in the synthesis and repair of bone collagen, and vitamin K is required for adequate formation of bone structure.

Among all vitamins, a special notion should be given to vitamin D, one of the most important nutrients related to osteoporosis. Its better known functions are to promote calcium and phosphorus absorption, and ensuring adequate bone mineralization. Vitamin D occurs in common foods such as dairy products (many milks are enriched in vitamin D), some fortified cereals, blue fish (including salmon, tuna, sardine, or anchovy), and eggs. Vitamin D may also be synthesized in our skin due to the action of sunlight upon it, although the amount synthesized depends on many other factors, such as the time of day or year or the latitude.

Studies show that vitamin D production is decreased in elderly or institutionalized persons (57-60). It has also been shown that, assuming a similar exposure time, vitamin D synthesis is lower in old age as compared to young adults or children. Skin conversion appears to be less effective in the elderly. Renal synthesis of 1,25-dihydroxyvitamin D is also impaired in this population group due to a decreased response to PTH. Finally, some resistance to the action of 1,25-dihydroxyvitamin D appears to exist at target organs (61). All of this results in a lower calcium absorption and a PTH elevation, which leads to an increased remodelling and mineralization loss.

For all of these reasons, men and women over 70 years of age are less likely to cover their vitamin D requirements with sun exposure. Elderly people need a greater intake of food containing vitamin D or vitamin D supplementation.

Vitamin D supplementation may prevent bone loss in the elderly (62). Moreover, studies show that the use of calcium and vitamin D decreases fracture risk. In a placebo-controlled study on 1634 women receiving 1200 mg/day of calcium and 800 U/day of vitamin D3 for 18 months, Chapuy et al. noted a 25% reduction in hip fractures (p=0.043) and a 15% reduction in non-vertebral fractures (p=0.015) (63). In another study by Dawson-Hugues et al, supplementation for 3 years with 500 mg of Ca and 700 IU of vitamin D decreased incidence of non-vertebral fractures by 50% (p=0.02) (64).

In addition, most studies showing antifracture efficacy with the different antiresorptive and bone-forming agents have included calcium and vitamin D supplementation, and the different antiosteoporotic drugs have been shown to be less effective when administered to patients with inadequate calcium and vitamin D levels. Thus, calcium and vitamin D supplementation should be given as an adjuvant therapy, added to any other anti-osteoporotic treatment (65).

Vitamin D doses currently recommended by the guidelines for elderly subjects are 700-800 UI/day (46,47). The available evidence also alerts about the importance of detecting vitamin D deficiency to be treated as part of a fall prevention program in the elderly (66).

#### 3.8 Flavonoids and others

Bone morphogenetic proteins (BMPs) stimulate bone formation, and the BMP2 gene has been found to be related to osteoporosis. The possibility of positive effects through dietary

sources, such as those rich in polyphenols that stimulate the BMP2 promoter and its effects on bone formation is currently being investigated. Flavonoids contained in certain food products may therefore promote bone formation It could thus be possible to improve bone mass by such dietary means and to decrease the risk of osteoporosis at these stages of life (67).

#### 4. Deficiencies and conditions affecting bone in the elderly

#### 4.1 Energy balance and body weight in the elderly

Intake and energy expenditure gradually decrease with age. Changes also occur in body composition, including loss of lean mass and increased fat. These modifications may be considered adjustments with the intention of prolonging life, including changes occurring in middle and old age.

From 30 years of age, the basal metabolic rate (BMR) has been reported to decrease by approximately 5 kcal/day/year, and energy intake by approximately 12 kcal/day/year. Lean body mass decreases by 2%-3% each year, and this decrease is mainly related to muscle mass loss (sarcopenia) (68). Loss of strength, and the resulting increase in propensity to fall, is much faster than the concomitant muscle mass loss. This suggests a difficult to reverse impairment in muscle quality. A mean 15% decrease occurs in total body water between the middle age and old age. Fat is redistributed around the trunk, being mainly deposited in the abdominal region, while subcutaneous and limb fat is decreased (69). Weight usually changes little, but may decrease by 10% between 70 and 80 years of age. It remains to be established whether lean body mass reduction is an adaptive mechanism to decrease activity level or is the consequence of the age-related decrease in physical activity. From the functional viewpoint, lean mass loss is associated to changes in many physiological functions (respiratory, gastrointestinal, immune, etc.). The etiology and purpose of changes in body composition in the elderly remain obscure and highly controversial.

15% to 20% of elderly people experience a weight loss defined as a 5% loss of their usual weight. This proportion reaches 27% in selected high-risk populations (old people with Psychosocial determinants and the higher prevalence of acute and chronic illnesses). In a study conducted in Spain on 450 subjects older than 65 years, 20% showed a weight loss greater than 4% at one year of follow-up (70).

The aging process involves changes in organs and systems that may influence intake decrease and weight loss in the elderly to a greater or lesser extent, thereby contributing to an increased bone demineralization and development of osteoporosis. Some of these changes and their relationship to nutritional status are discussed in detail below.

#### 4.2 Changes in special senses

Taste and smell start to decline at about 60 years of age, with losses being more severe at 70 years (71). Not only aging itself may affect these senses, but also some drugs commonly used in the elderly (digoxin and theophylline), nutritional deficits (zinc, niacin, etc.), associated diseases such as Bell paralysis, multiple sclerosis, Sjögren syndrome, glossitis, etc. Loss or decrease in these senses is important, because when stimulated they induce increases in salivation and gastric and pancreatic secretion.

Decreased hearing, vision, and coordination may result in a decreased intake by causing loss of appetite and food recognition and impair the intake process. Senile cataract is also a significant problem as a cause of vision loss in elderly people. Antioxidant nutrients including vitamin C, carotenoids, and vitamin E and their potential relationship to senile cataract have been studied (72). High carotenoid levels in plasma have been reported to be related to a delayed cataract formation. It is thought that vitamin E could play a significant role in the maintenance of the integrity of cell membranes of the lens of the eye. Vitamin C levels are 30 times higher in the lens as compared to plasma; however, subjects with cataract or elderly people have low vitamin C levels in the lens, particularly in the nucleus, which is where senile cataract starts (73). Some studies found a lower incidence of cataract in people with high vitamin C levels of ca. 80 µmol/L (maximum plasma vitamin C saturation) as compared to those with 40  $\mu$ mol/L, but very high doses of vitamin C (> 1000 mg/day), which are rather pharmacological than nutritional and then may be harmful, are required to reach those levels (74-76). Further studies are required to ascertain whether, as some studies appear to suggest, dietary changes, i.e. diets rich in antioxidant systems, may prevent occurrence or progression of cataract, which is a significant cause of morbidity and disability, and also involves significant healthcare costs.

#### 4.3 Changes in the oral cavity

Virtually 70% of elderly subjects have xerostomy or a dry mucosa, which clearly affects food intake. Periodontal disease, tooth loss, and presence of dentures, so common in the elderly, impair adequate food salivation and subsequent swallowing (77).

A study conducted by Posner et al. (78) found a close relationship between dental disease and malnutrition in the elderly population. This is an easily treatable cause of malnutrition.

#### 4.4 Gastrointestinal changes

Changes affecting the ability to digest and absorb food occur during normal aging. Hypochlorhydria, that may promote bacterial overgrowth and also impair vitamin  $B_{12}$  absorption, causing pernicious anemia and mental changes, is not uncommon from 60 years of age (39).

At about 50-60 years of age, calcium transport mechanism is impaired, and calcium absorption is therefore decreased.(40). Use of excessively fiber-rich diets, which are in fashion today, may contribute to a lower absorption of this mineral, albeit fiber rich foods are usually also rich in dietary minerals, and the effect of fiber to increase mineral absorption in the large intestine is still not completely understood. A lactase deficiency is not uncommon in elderly people.(79). When faced with this situation, rather than removing dairy products from the diet, which would decrease calcium intake, it is essential to recommend the use of dairy products treated with lactase or fermented products (yogurt, junket).

Adult celiac disease is a cause of malnutrition in this population group more common than usually thought, and is therefore a diagnosis to be considered (80). Adult celiac disease may cause few symptoms, but is associated with discomfort and/or pain related to food intake, so that this is voluntarily decreased, which may cause weight loss and micronutrient deficiencies. Gluten-free diets prevent these symptoms.

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Constipation is very common in the elderly population. It is related to an inadequate food intake distributed in few meals, to inadequate fluids, and to the presence of depression (81) Use of laxatives in the elderly has been independently associated with the occurrence of hypoalbuminemia.

#### 4.5 Cardiovascular changes

Cardiovascular disease currently accounts for 70% of deaths in people over 75 years of age, who have a greater prevalence of high blood pressure and hypercholesterolemia as compared to young adults. Some studies have shown therapeutic diets in patients with hypercholesterolemia and HBP to cause weight loss, hypoalbuminemia, and orthostatic hypotension (which may in turn cause falls in an already susceptible population) (82,83).

#### 4.6 Renal changes

Kidney function may decrease 50% between 30 and 80 years of age. Elderly subjects have a poorer management of acid-base changes and protein and electrolyte overload. Some authors suggest that geriatric nephropathy could be the result of excess protein consumption throughout life (84). In fact, mean protein consumption in the United States is 166% of the RDAs, and consumption is too high in the whole Western society. Thus, additional intake over the recommended 1-1.25 g/kg intake of proteins per day in elderly subjects may not be encouraged.

#### 4.7 Musculoskeletal changes

As already discussed, fat mass increases and lean body mass is lost during the normal aging process, so that healthy elderly people have a 30%-40% lower proportion of body protein (including muscle mass). The loss involves both the somatic and visceral compartments. Fat is mainly deposited in the trunk. Height loss due to vertebral fractures induced by osteoporosis is common in the elderly. Elderly women tend to restrict calorie intake to a lesser extent than men. Waist-hip ratio tends to be higher in males of a similar age and BMI.

Muscle changes associated with old age may be responsible for the decreased energy expenditure seen in the elderly. These changes are not reversed with dietary measures, but may be reversed with regular exercise. Physical activity helps maintaining integrity of skeletal muscle and bone, and also reduce the risk of falls and fractures. An adequate and balanced diet is indispensable to maintain an adequate muscle function. An inverse relationship has been seen between muscle strength and circulating vitamin D levels, and the presence of vitamin D receptors in muscle and the positive action of vitamin D on muscle metabolism are known (85). Studies have shown that calcium and vitamin D supplementation reduces the risk of falls in the elderly, probably as the result of increased muscle strength and maintenance of neuromuscular coordination. The association of calcium and vitamin D is more effective than vitamin D alone for reducing the risk of falls in women over 70 years of age (86). A group of elderly women were administered calcium 1200 mg/day plus vitamin D 800 IU, and another group received calcium alone for 12 weeks. The calcium and vitamin D group experienced a 49% decrease in the risk of fall as compared to the group on calcium alone, in relation with the improvement of muscle function (87).

#### 4.8 Neurological changes

Neurological changes are very common in the elderly and may have a great impact on their nutritional status. For instance, tremor from Parkinson's disease, motor deficits induced by stroke, Alzheimer's disease, or other type of dementia may seriously impair intake. Experimental use of substances that may act as precursors for altered neurotransmitters in conditions such as Parkinson's or Alzheimer's disease is of great interest, although the role of these nutrients, such as tyrosine, tryptophan, and choline still remains to be fully elucidated.

A potential interesting relationship is the established one between carbohydrate-rich, low protein diets and attention deficit and a decreased alert status in elderly people. This could be due to a decreased serotonin synthesis.(88)

#### 4.9 Immune system changes

Healthy elderly people experience, rather than a decreased immune response, a dysregulation inducing changes in both humoral and cellular immunity (89). Malnutrition is a factor that may induce a decreased immune response. Lymphocyte count in peripheral blood usually decreases by 10%-15% with age (90). Not only the number, but also the type is modified, so that there is a predominance of immature lymphocytes, natural killer (NK) and T helper 2 (TH2) cells, with a decrease in T helper 1 (TH1) cells. In vitro studies show a lower reactivity of lymphocytes from elderly people upon exposure to lectin or antigen stimulation. Thus, peripheral blood lymphocytes from elderly subjects have a lower capacity to respond to different stimuli as compared to those from young people.

These changes are probably responsible for the decreased cell-mediated immunity seen in the elderly. Energy and protein malnutrition also induces changes in cell immunity in the elderly that makes them more susceptible to lung infections (91).

In the elderly, malnutrition also induces changes in the function of polymorphonuclears and monocytes, and may therefore modify clinical symptoms of inflammation. Thus, an infected and malnourished elderly subject may not experience fever due to the poor release of interleukin-1. Lack of cytokine release results in a decreased mobilization of body reserves in the malnourished elderly, which causes an inadequate nutrient supply to lymphocytes, which further impairs the defense mechanisms. Some studies have shown that the intake of dietary supplements is able to reverse the majority of changes seen in cell-mediated immunity (92).

Aging also modifies humoral immunity. An increased antibody response appears to occur in the elderly, as shown by the fact that the levels of some immunoglobulins and monoclonal antibodies are increased. However, elderly people have a lower, shorter, and slower response to primary immunization as compared to young people (93).

In addition, antibodies from elderly people have less affinity for antigens and a reduced action spectrum as compared to young people. Long-term exposure to antigens during the life may be responsible for the impaired immune response seen in old age. Malnutrition further impairs this response, so that the absence of response to immunization in hospitalized elderly individuals has been attributed to malnutrition in 75% of cases (94).

As in humoral immunity studies, use of dietary supplements in malnourished elderly patients improves antibody response (92). They may therefore be indicated in such patients before they are vaccinated. A study where yogurt (95) was used as a supplement to the usual diet of subjects enrolled showed an improvement in immunological indices while supplementation was maintained, but energy intake continued to be low. We may therefore speculate about the role of calcium in such improvement.

#### 4.10 Anorexia in the elderly

Elderly people appear to have an impaired appetite regulation and response to food intake that, among other things, causes a greater difficulty as compared to young adults to recover their initial weight after a weight loss or gain. The elderly tend to satiate earlier than young people after a meal; this early satiety is thought to be the consequence of signals emitted from the stomach. Most studies agree that a slower gastric emptying and a faster passage from the gastric fundus to the antrum occur with age (96). Food therefore remains in the antrum for a longer time, inducing a greater gastric distention.

Cholecystokinin, the major satiating hormone par excellence, may influence decreased intake in the elderly, particularly when malnourished, in whom it is secreted in greater amounts after food intake as compared to young subjects. However, further studies are required to elucidate the role of this hormone in age-related decrease in food intake.

Stimulation of  $\kappa$  opioid receptors by dynorphin plays a significant role in fat intake both in animals and humans. The number of opioid receptors decreases with age (97), which may explain the decreased fat consumption with age, much in the same way as hypodipsia in the elderly has been related to an age-related decrease in the number of  $\mu$  opioid receptors.

Sex hormones also influence food intake, which is increased by testosterone and decreased by estrogens (98). Age-related decrease in intake is lower in women as compared to men, which may be related to the decrease in estrogen levels occurring in menopause. In men, testosterone levels decrease with age, which may lead not only to a decreased intake, but also to the loss of lean mass and the gain of fat mass predominately in the trunk reported in elderly males.

Leptin is a recently reported hormone, the product of the ob gene and synthesized by adipose tissue (99). Leptin serum levels are therefore related to the amount of body fat. Leptin concentrations tend to decrease with age, which suggests that the leptin signaling system may be impaired with time. This decrease may be the result of a decreased production and/or an increased clearance (100). Thus, leptin may also play a role in age-related anorexia.

#### 4.11 Polymedication and treatment compliance

Elderly patients have a high incidence of comorbidities requiring long-term concomitant use of several drugs. This influences bone health in two aspects, one of them directly derived from the harmful side effect on bone metabolism of some drugs such as corticosteroids, glitazones, heparins, antiepileptics, etc. On the other hand, compliance with treatment against bone mass loss is difficult, with frequent discontinuation of calcium and vitamin D supplements, but also of specific treatments such as bisphosphonates, strontium salts, teriparatide, etc. (101).

#### 4.12 Psychosocial changes

Unfortunately, frequent causes of malnutrition in the elderly population include short financial resources at the end of active working life and the social isolation faced by many elderly individuals in Western society. In elderly patients, depression is a much more frequent cause of malnutrition than in young people. Depression may cause malnutrition due not only to the anorexia usually associated with it, but also because of the loss of the capacity to enjoy social events, which very often occur around a table (102).

Furthermore, elderly people may have significant difficulties to buy food as a consequence of concomitant diseases affecting their mobility and/or strength.

#### 5. Conclusions

Bone mass, one of the main components that determine bone strength, the reduction of which characterizes osteoporosis, experiences a gradual physiological decrease with age, and reach lower levels in the elderly. To this physiological loss should be added the negative effect caused by the decreased plasma levels of gonadal hormones and other factors, including nutritional deficiencies or changes conditioned by functional status and the presence of other concomitant diseases, such as endocrine and rheumatic diseases, the use of some drugs, etc.

Nutrition should be balanced during the elderly period of life, and adequate calcium intake, with or without vitamin D supplements, would attenuate bone mass loss. Other recommendations to be considered include avoidance of a high protein content in the diet, due to its high phosphate content; avoidance of strict vegetarian diets, especially vegan diets, because of their high phytate and oxalate contents, and also due to their relatively low content of some vitamins.

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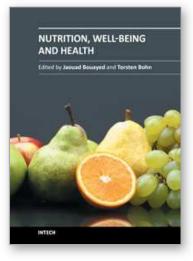
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#### Nutrition, Well-Being and Health

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In our modern society, expectations are high, also with respect to our daily diet. In addition to being merely "nutritious", i.e. supplying a variety of essential nutrients, including macro-nutrients such as proteins or micronutrients such as minerals and vitamins, it is almost expected that a good diet offers further advantages especially well-being and health and the prevention of chronic diseases, which are, as we generally tend to grow older and older, becoming a burden to enjoying private life and to the entire society. These additional qualities are often sought in diets rich also in non-nutritive components, such as phytochemicals. In contrast to drugs, which are taken especially to cure or ameliorate diseases, it is expected that a healthy diet acts in particular on the side of prevention, allowing us to become old without feeling old. In the present book, rather then trying to give an exhaustive overview on nutritional aspects and their link to well-being and health, selected topics have been chosen, intended to address presently discussed key issues of nutrition for health, presenting a reasonable selection of the manifold topics around diet, well-being, and health: from the antioxidants polyphenols and carotenoids, aroma-active terpenoids, to calcium for bone health, back to traditional Chinese Medicine.

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