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THE DIRECTOR GENERAL

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OPINION

of the French Food Safety Agency on the assessment of nutritional needs for frail elderly people and those suffering from certain pathologies, in order to establish nutritional references and provide appropriate nutritional support.

Overview of the internal request

The French Food Safety Agency (Afssa) issued an internal request on 20 September 2008 to assess the nutritional needs of frail elderly people and those suffering from certain pathologies in order to define nutritional references and provide appropriate nutritional support.

Background information and working objectives

This study follows on from previous work on the identification of populations with particular nutritional requirements (Amended Decree of August 29, 1991). In its opinion issued on 11 June 2008, Afssa's position was that frail elderly people could be characterised as a target population for foodstuffs intended for particular nutritional uses based on the following elements:
"[...] at a given age, there is a *continuum* of situations ranging from normal health to evident illness and, conversely, a clinical situation can correspond to a population of different ages. For these reasons, this paragraph will deal with frail elderly people aged 75 years and over.
Ageing results in lower dietary intake due to quicker satiety (Morley, 2002; Ferry, 2007), appetite dysregulation and secondary nutritional problems from previous illnesses. The nutritional requirements of elderly people are defined by RDIs (Cynober *et al*., 2001). They are at least equal to those of younger adults in amount (per kg of body weight), except for energy, and in quality. Since spontaneous consumption in frail elderly people is reduced, foods intended for normal consumption are not sufficient to cover their requirements.
This consumption deficit is one of the key mechanisms of function and weight loss, and increases frailty."

The aim of this study is therefore to define nutritional references providing appropriate nutritional support for frail elderly people and/or those suffering from certain pathologies. It is based on the data in the literature relating to nutritional requirements and clinical studies on dietary intervention in these individuals.
The pathologies taken into account have been identified as 1) frequent in elderly people, 2) closely related to nutritional status and 3) having sufficient supporting data in the literature. These pathologies include Alzheimer's disease, pressure sores, hip fractures and infections.

This study will not deal with nutritional support for pathologies associated with ageing, such as cardiovascular disease or age-related macular degeneration.

For each physiopathological situation, the scientific bases on which the nutritional references are founded (physiopathological arguments, clinical study data, consensus of experts) are explained. In the absence of sufficient data to define these nutritional references, the French population reference intakes (ANCs) for healthy elderly subjects are considered to be valid for frail elderly people.

After consulting a working group made up of geriatric experts and validating the conclusions by the "Human nutrition" Scientific Panel at its meeting on 27 March 2008, Afssa issued the following opinion:

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Reasoning

1. Introductory elements

The thresholds chosen for defining elderly people vary depending on the authors and periods. With increased life expectancy, the threshold of 65 years – in application several years ago – no longer appears to be relevant. In accordance with recent data on the nutrition of elderly people, ages 70 or 75 are now taken as thresholds.

Elderly people are an extremely heterogeneous population in terms of health. Although the definitions of frailty vary from author to author, it can be taken that "frail" elderly people are people with an increased risk of morbidity, functional dependency, hospitalisation, entry into residential care or mortality (Hogan et al. 2003). All authors agree that undernutrition is an important criterion for frailty. With frail elderly subjects, it is certainly particularly important to ensure the effectiveness of nutritional interventions, with the aim of preventing worsening of their state of health, autonomy and social situation.

Ageing is accompanied by changes in body composition with, in particular, progressive loss of muscle mass, known as sarcopenia (Baumgartner et al. 1998). This is due to multiple causes, including sedentary lifestyle, insufficient protein intakes, impaired protein metabolism, neurodegenerative processes, reduced production and activity of anabolic hormones and secretions of proinflammatory cytokines (Walrand et al. 2005). Sarcopenia is associated with reduced muscle strength, dependency, walking difficulties and the risk of falling (Borst 2004, Szulc et al. 2005). In elderly subjects, to a more pronounced degree than in younger adults, undernutrition is accompanied by a loss of weight to the detriment of muscle mass, worsening sarcopenia still further (Schneider et al. 2002).

Furthermore, food intakes decrease in a linear manner during the course of life (Wakimoto & Block 2001). Even in good health, elderly people whose weight is stable have less appetite, prior to eating, than young subjects, and after a normal meal they have a greater feeling of satiety. This is "age-related anorexia" (Morley 2002). The mechanisms involved are complex and not yet fully understood. Impaired sensory capacities, such as the higher taste and smell threshold associated with ageing, may be involved, as may the slowing down of gastric emptying, or increased production of anorexigenic factors (in particular cholecystokinin) and decreased production of orexigenic factors (growth hormones, neuropeptide Y, etc.) (Wilson & Morley 2003). Some of these changes can be interpreted as adaptive phenomena enabling a stable weight to be maintained despite a decrease in energy requirements (less physical activity, decreased muscle mass), but they can upset nutritional balance, compromising the individual’s capacity for adaptation and compensation during periods of under-eating. The work of S. Roberts (1994) has clearly shown that after a period of under-eating (800 kcal/day less than the usual daily ration for three weeks), young subjects go through a phase of hyperphagia to compensate and regain their original weight. On the contrary, elderly subjects, after the same period of under-eating, were incapable of spontaneously increasing their food intake and did not regain their healthy weight. These results were confirmed by a longer-term study (Moriguti et al. 2000). This illustrates the difficulty for elderly subjects who have suffered from psychological stress or an acute medical episode - usually associated with decreased food intake and weight loss - to regain their previous weight spontaneously.

In this weakened state, many different interconnected factors can combine to trigger or worsen undernutrition; these may be pathological (an acute pathology or decompensation of a chronic pathology), psychological or social, and may be worsened by drugs and certain diets (Ferry et al. 2007). The main risk factors for undernutrition (anorexia, an acute pathology or psychological stress, depression, dementia, loss of autonomy in terms of mobility or eating, polymedication, pressure sores, etc.) are included in the Mini Nutritional Assessment questionnaire (MNA™), which is a recommended tool for undernutrition screening in elderly people within the framework of the PNNS (French National Health Nutrition Plan).

Diagnosis of undernutrition is based on anthropometric and biological criteria or the MNA^{TM} score. Just one of the following criteria is sufficient for diagnosing undernutrition in an elderly person:

- weight loss ≥ 5% in 3 months, or ≥ 10% in 6 months;
- body mass index (BMI) < 21;
- albuminemia < 35 g/l;
- MNA^{TM} score < 17.

The major epidemiological studies conducted in Europe (Euronut-Seneca 1991 and 1996) and the United States (NHANES I and II) show that 4 to10% of elderly people living at home suffer from undernutrition. In elderly people living at home but requiring home help, the prevalence of undernutrition may be as high as 25 to29% (Christensson et al. 1999, Odlund et al. 2005). In residential care, this prevalence varies between 19 and 38% (Sayoun et al. 1988, Margetts et al. 2003, Crogan & Pasvogel 2003). Finally, in hospital, where the effects of polypathology, pain, psychological distress and sometimes insufficient nutritional support are combined, the prevalence of undernutrition may be as high as 30 to90% of elderly patients (Constans et al. 1992, Thomas et al. 2002, Pablo et al. 2003, Paillaud et al. 2004).

It has been clearly shown that protein-energy undernutrition in elderly people is associated with increased mortality in an urban environment (Corti et al. 1994, Wallace et al. 1995, Payette et al. 1999, Raynaud-Simon et al. 2002) and in hospitals (Sullivan et al. 1991 et 1999, Herrmann et al. 1992), with longer stays in hospital (Herrmann et al. 1992), with nosocomial infections (Potter et al. 1995, Paillaud et al. 2005), with the appearance of pressure sores (Berlowitz & Wilking 1989, Bergström & Braden 1992, Reed et al. 2003, Stratton et al. 2005), and with falls and fractures (Ensrud et al. 1997, Lumbers et al. 2001).

Finally, various deficiencies in micronutrients have been noted in the elderly population. In the population living at home included in the Euronut – SENECA study (1991 and 1996), plasma vitamin B_6 concentrations were low in 5.7-23.3% of subjects, as were those of vitamin B_{12} in 2.7-7.3% of subjects, and those of vitamin D in 36-47% of subjects. In 23.9% of men and 46.8% of women, food intake was low for at least one of the following micronutrients: calcium, iron, vitamin A1, ß-carotene, thiamine, pyridoxine or vitamin C. In elderly people in residential care, deficits in micronutrients appear to be even more frequent (Lowik et al. 1992). However, the effect on the health of these moderate deficits in micronutrients is still not properly understood.

2. Definition of nutritional references for frail elderly people

2.1. Concepts

Different types of ageing have been described: successful, normal and pathological.

Successful ageing is characterised by a condition with no functional restrictions, no cognitive loss and with no diseases liable to threaten a vital prognosis including cardiovascular disease, obstructive broncho-pneumopathies, asthma or cancer (Newman et al. 2003). A social aspect should be added to this definition: continuing to take part in social activities is another criterion of successful ageing, although this concept is not limited to the elderly (WHO 2001).

Conversely, pathological ageing involves irreversible damage to one of these components, in particular functional dependency for the basic acts of daily life, represented by the need for help with walking, going to the toilet, washing, dressing, eating and continence.

Normal or usual ageing represents all the intermediary states.

In practice, the use of this classification is limited by the many different definitions of frailty given by different authors and in different areas. The social consequence of pathological ageing is seen as entry into residential care and the failure to maintain care at home. It should be noted however that age itself is the greatest risk factor for pathological ageing (Newman et al. 2003). Furthermore, among a cohort of 100-year-olds with so-called successful ageing, none had maintained a social role in spite of the absence of dependency or any disabling chronic pathology (Motta et al. 2005). Finally, very elderly people (over 85) deal with these pathologies better than younger individuals (Idler 1995) and even with functional dependency, which they consider to be normal for their age (Baberger-Gateau et al. 1992).

Fragility represents the intermediary states between normal and pathological ageing. Fragility could be defined as an increased risk of morbidity, functional dependency, hospitalisation, entry into residential care or mortality (Hogan 2003). This is not a well defined category but rather an array of different states (Hamerman & Toward 1999). Vulnerability is a fairly closely related concept in which age-related loss of homeostasis is considered (Hogan 2003). A physical and mental deficiency is also mentioned as well as a lack of social activity. The subject, faced with a new life event such as a fall or a serious infection, cannot cope with this new situation and the dependency caused by the new event risks worsening. The frail elderly subject must therefore be identified in order to implement preventive measures against loss of autonomy and the deterioration of their mental and social situation.

2.2. Nutrition and frailty

According to all authors, protein-energy undernutrition is a major cause of frailty, all the more so because it is associated with a loss of muscular mass and muscle weakness, with an obvious impact on muscle function. Low muscular mass is associated with the risk of functional decline (Janssen 2006). Undernutrition is strongly linked to the risk of falling (Vellas et al. 1992). Hospitalised elderly people with a calorie intake of less than 600 kcal/day or who have had a fall have a higher risk of being taken into residential care (Bourdel-Marchasson et al. 2004). Among the nutritional markers, weight loss appears to be a more important predictive factor of functional decline and mortality than a low body mass index (BMI) (< 23.5kg/m2) or a daily calorie intake of less than 1800 kcal/day (Chin et al. 1999).

However, obese subjects (BMI> 30kg/m2) are not exempt from functional decline, in particular due to motor difficulties caused by excess weight, and also due to an unfavourable body composition with an excess of fatty mass compared to muscular mass, this situation being worsened by restrictive diets combined with a lack of physical exercise (Bourdel-Marchasson et al. 2004).

The other clinical criteria for fragility are chronic pathologies, principally including Alzheimer's disease and other forms of dementia, depression, cerebrovascular pathology, diabetes, cancers, as well as polymedication, chronic inflammatory states, deficiencies such as incontinence, sensory impairment, sensitivity to drug side effects, and finally events such as falls, pressure sores and confusion-like syndromes or disorders (Bourdel-Marchasson & Berrut 2005).

Standard gerontological assessment applied to frail subjects makes it possible in the best of cases to prevent loss of autonomy. By assessing the individual’s cognitive, emotional, nutritional and functional states, pathologies (treatments and impairments) and social situation, it becomes possible to prevent entry into high-dependency care (Rainfray et al. 2002). Among these factors, nutritional support is an important element.

2.3. Nutritional support of frail elderly subjects

2.3.1. Energy requirements

Energy requirements are defined by WHO (2005) as the quantity of energy needed by an individual to maintain a weight and body composition which is compatible with a good long-term state of health, and physical activity engendering satisfactory economic and social activity. This definition does not include adjustments for age, fragility, or illness. WHO recommends that energy requirements should be assessed in terms of the energy used in a 24-hour period.
The energy expenditure at rest of healthy elderly people decreases with age, proportionally to the loss of lean mass. Physical activity also decreases with age. The physical activity level ((PAL), defined by the ratio of total energy expenditure to energy expenditure at rest, DRI 2001)

is 1.42 in average (Gaillard et al. 2007). The notion of "physical activity engendering satisfactory economic and social activity" used by WHO is probably irrelevant in that elderly people no longer work. Furthermore, as stated previously, their social involvement may not be a good criterion for assessing successful ageing. This consideration should be replaced by a functional parameter: "maintained physical activity for functional autonomy" which would involve taking into account the additional energy requirements arising from this physical activity, i.e. to develop sufficient muscular mass for these functions and those induced by the increase in lean mass.
Despite the small number of studies on the subject, it is thought that energy expenditure at rest for ill elderly people is not greater than that of healthy elderly people. The energy expenditure is the same for men and women, and can be estimated at 19 kcal/kg of weight/day (Gaillard et al. 2007). It does not vary with pathologies causing short stay hospitalisations (for the most common pathologies). There is little reason to believe that this energy expenditure increases with Alzheimer's disease or dementia, or in the event of moderate inflammation or grade 1 and 2 pressure sores (Dambach et al. 2005). This energy expenditure at rest is higher for patients with a BMI of less than 21kg/m² and for individuals over 100 years of age, with no explanation for this finding. For a physical activity level (PAL) of 1.3-1.5 (sedentary subjects with normal activities), the minimum energy requirements for ill elderly people are 25-30kcal/kg/day for patients with a BMI of over 21, and 28-32 kcal/kg/day for patients with a BMI of less than 21. This is the minimum requirement for these patients to maintain the reduced physical activity and weight levels compatible with their illness. It is very likely that higher energy requirements would be necessary in order to achieve an improvement in the patient’s strategic functions regarding their pathology (for example, the healing of pressure sores) or environment (recommencing satisfactory physical activity, see above).

Thus the energy requirements of frail elderly people are very probably covered by the ANCs for elderly people in general, i.e. 36 kcal/kg/day (Cynober et al. 2001). This objective may be adjusted by 30 to 40 kcal/kg/day, according to individual nutritional status, corpulence and levels of physical activity.

2.3.2. Protein requirements

Protein requirements for healthy elderly people remain a subject of controversy and there is insufficient knowledge regarding those for frail elderly people.
For healthy elderly populations, the recommendations are 0.80g/kg/day for the WHO (FAO/OMS/UNU 1985) and the "US and Canadian Dietary Reference Intake" (2002). ANCs of 1g/kg/day are recommended for the healthy elderly population (Afssa 2007, Cynober et al. 2001). Data in the literature relating to protein requirements for healthy or frail elderly subjects suggests that 1 to 1.3g/kg/day of protein are necessary to maintain their nitrogen balance; the authors propose that protein intake should reach at least these levels for frail elderly subjects (Morais et al. 2006).

A recent study on elderly people aged 66-99 admitted to hospital for an acute pathology shows an average requirement of 1.06 ± 0.28g/kg/day and therefore "safety" protein intakes (1.06 + 2 standard deviations) of 1.6g/kg/day (Alix et al. 2006). In fact there is little available data on measuring the nitrogen balance of elderly people (Scrimshaw et al. 1976, Uauy et al. 1978, Zanni et al. 1979, Cheng et al. 1978, Gersovitz et al. 1982, Kurpad & Vaz 2000). However, several arguments plead in favour of increased protein requirements in the elderly. Energy intakes decrease with age: it is conceivable that to compensate for the lack of nitrogen retention associated with these low energy intakes, protein must account for a greater proportion of total energy intake, to an extent which remains to be specified. Furthermore, damage to the regulation of protein synthesis and proteolysis has often been reported in elderly people. This is principally a reduction in protein turnover in response to anabolic stimuli.
Thus ageing is associated with reduced protein synthesis in response to an intake of amino acids and glucose (Volpi 2000), but this protein synthesis may be restored by increasing amino acid intake (Volpi 1999).
There is only one study specifically addressing the question of protein requirements in frail elderly people (Bunker et al. 1987). In this study, the nitrogen balances of 24 healthy elderly people were compared to those of 20 housebound elderly people, suffering from various chronic pathologies, with home helps or meals on wheels. The nitrogen balances of the healthy elderly

people were balanced with protein intakes of 0.97g/kg/day. The frail elderly people had a negative nitrogen balance with protein intakes of 0.67g/kg/j and lower calorie intakes. Unfortunately this type of study does not enable an desirable level of protein intake to be recommended for frail elderly people.
Nevertheless, it can be supposed that the protein requirements of frail elderly people are often probably covered by intakes of 1g/kg/j, as is the case for elderly people (Afssa, 2007). However, in the case of undernutrition or acute pathology, and in spite of the lack of data in the literature, we propose higher protein intakes of 1.2 - 1.6g/kg/day.

2.3.3. Oral nutritional support

After correction, if possible, of nutritional risk factors (suppression of specific diets, dental treatments, help with meals, treatment of pathologies, etc.), oral nutritional support includes the following:

- nutritional advice, regarding meal frequency (3 meals with sufficient time between them plus 1 or 2 snacks per day) and make-up (a varied diet, including five servings of fruits and vegetables per day, carbohydrates at each meal, foods with a high protein content twice a day and dairy products three times a day (French National Health and Nutrition Programme, PNNS);
- a diet enriched with everyday foods (eggs, grated cheese, powdered milk, oil, butter, fresh cream, etc.), in order to boost the nutritional density of dishes without increasing volume;
- oral nutritional supplements. These supplements are savoury or sweet and are available in a wide range of textures (liquids, creams, etc.) and flavours. High-energy and high-protein products are likely to be the most effective for increasing food intakes.

An enriched diet is effective for increasing nutritional intakes of frail elderly people in residential care (Odlund Olin et al. 2003). However, the majority of clinical studies on oral nutritional support use oral nutritional supplements, packaged in such a way as to provide standardised intakes. These oral nutritional supplements boost energy and especially protein intakes (Potter et al. 2001, Bourdel-Marchasson et al. 2000).

Therapeutic trials on the effectiveness of oral nutritional support for elderly people have been the subject of systematic review and meta-analyses (Potter et al. 2001, Milne et al. 2002, Milne et al. 2006). The most recent meta-analysis (Milne et al. 2006) examines the findings of 55 randomised therapeutic trials (n = 9187 subjects) conducted at home, in hospital and in residential care and shows that oral nutritional support provides the following:

- weight gain in elderly people living at home, in residential care or during short stay hospitalisation (a 2.13% increase in body weight [confidence interval CI 95% 1.78 - 2.49]);
- reduced risk of complications in elderly people during short stay hospitalisation (OR = 0.72 [0.53 – 0.97]);
- reduced risk of mortality in elderly people defined as suffering from undernutrition during short stay hospitalisation, (OR = 0.66 [0.49 – 0.90]).

Implementation of a standard screening and oral nutritional support programme has made it possible to significantly reduce the length of hospitalisation in geriatric units (Pepersack 2005). However, the meta-analysis of clinical studies relating to the effectiveness of oral nutritional support shows only a trend towards reducing the length of stay (- 1.17 days [CI 95% -3.90 – 1.57]) (Milne et al. 2006).

Few studies report decreased morbidity and mortality in elderly people due to oral nutritional support (Milne et al. 2006). However, in an out-patients population defined at being at risk of undernutrition by the MNA™, the prescription of oral nutritional supplements was associated with significantly lower medical costs (Gazzotti et al. 2003).

2.3.4. Artificial nutrition

The indications for enteral nutrition are the same in elderly people as for other adults: enteral nutrition is an option in cases where oral nutrition is impossible, contraindicated or insufficient, as long as the digestive tract is in proper working order. Parenteral nutrition is used only in the following three situations: severe anatomical or functional malabsorption, acute or chronic intestinal occlusion and failure of properly implemented enteral nutrition.

For ailing elderly people, the clinical benefit of enteral feeding depends on their pathological condition.

In undernourished elderly patients, enteral nutrition makes it possible to improve nutritional status (Hébuterne et al. 1995; Abitbol et al. 2002), although progress is slower than in younger adults. In elderly people in residential care who are totally dependent in terms of feeding or who suffer from swallowing disorders, enteral nutrition has reduced the mortality rate (Rudberg et al. 2000).

However, in elderly people, enteral nutrition is usually used to remedy feeding problems resulting from strokes, dementia and other neurodegenerative diseases; it is often used in the case of patients with serious chronic dependency (Howard & Malone 1997, Bourdel-Marchasson et al. 1997).
Thus some authors report a lack of improvement in nutritional status with enteral nutrition (Ciocon et al. 1988; Henderson et al. 1992; Callahan et al. 2000; Silver et al. 2004). Furthermore, in these elderly populations, there appear to be frequent complications with enteral nutrition (agitation, pulling out the tube, obstructed tube, breathing pneumopathies, etc.) (Ciocon et al. 1988, Silver et al. 2004).

Because of this, the decision to prescribe enteral nutrition may be difficult for elderly people, especially if they are dependent and suffering from several pathologies. It may be thought that the clinical benefit will be greater if undernutrition is recent and results from a reversible pathological factor, and if enteral nutrition is proposed in view to returning to a previous clinical state. When undernutrition results from irreversible pathologies, associated with stabilised high dependency, enteral nutrition has not proved its effectiveness in terms of improvement of the quality or duration of life; the decision to prescribe or not to prescribe enteral feeding depends on a range of medical and ethical considerations.

2.3.5. Physical exercise

In elderly people living at home or in residential care and defined as being frail, resistance exercise improves strength and muscle function (Fiatarone et al. 1994, Binder et al. 2002, Bonnefoy et al. 2003). After hospitalisation for an acute pathology, physical exercise increases muscle strength and improves functional autonomy (Melin & Bygren 1992, Sullivan et al. 2001). Finally, in severely undernourished elderly people, physical exercise on a treadmill, at increasing speed and slope, 3 times a week for 3 weeks, led to increased spontaneous physical activity and VO_2 max (Bermon et al. 1997). In addition to the effect on muscle mass and function, physical exercise is liable to increase the effectiveness of nutritional support: in elderly people in residential care receiving a nutritional supplement, the daily amounts of foods ingested were significantly higher in the exercise group (Fiatarone et al. 1994). In frail elderly subjects benefitting from the administration of oral nutritional supplements, physical exercise enabled lean mass to be maintained (de Jong et al. 2000). Finally, nutritional support optimises the effectiveness of a physical exercise programme: in elderly men, during a 12-week physical exercise programme, the administration of a nutritional supplement engendered a significant increase in muscle mass (Meredith et al. 1992).

Physical exercise and nutritional support have a synergistic and complementary effect on an individual's nutritional status and functional capacities. For this reason, physical exercise, when adapted to the specific capacities of each elderly person, must be considered an integral part of a nutritional support programme.

In conclusion:
In frail elderly subjects, nutritional intervention is liable to be effective for maintaining or improving their nutritional status and functional autonomy.
In the absence of undernutrition, protein and energy requirements are most likely covered by the ANCs for healthy elderly people, i.e. 36 kcal/kg/day and 1g/kg/day or protein. Dietary guidelines, in particular those established for elderly people in the PNNS, may help with the practical application of this advice.
In the case of undernutrition, ANCs may be as high as 40 kcal/kg/day and 1.5g/kg/day of protein, according to the nutritional status, corpulence (BMI), physical activity and nutritional response to nutritional support. Dietary advice, fortification of meals or oral nutritional supplements is usually sufficient for improving nutritional status. If they are insufficient, enteral nutrition must be considered. Finally, to improve the nutritional and functional status of frail elderly people, nutritional support appears to be all the more effective if it combines diet and physical exercise.

3. Setting nutritional references for elderly people suffering from a pathology

The pathologies under consideration in this chapter are the following: Alzheimer's disease, pressure sores, hip fractures and bronchopulmonary and urinary infections.

3.1. Alzheimer's disease

The data from the PAQUID study (Ramaroson et al. 2003) makes it possible to estimate that over one in six people aged 75, i.e. 700,000 people in France, suffer from dementia, the most frequent form of which is Alzheimer's Disease (AD). AD is a degenerative pathology characterised by a gradual decline in cognitive functions, dependency and behavioural disorders. It is often accompanied by weight loss and undernutrition, factors which exacerbate the disease.

3.1.1. Weight loss and Alzheimer's disease

Weight loss is common in subjects suffering from AD; it occurs at all stages of the illness. Weight loss may occur in the early stages of the disease, even before a diagnosis of cognitive disorders is made (Barret-Connor et al. 1996, Stewart et al. 2005). It is thought to affect 30% of patients presenting mild to moderate AD (White 1996) and 50% of dementia patients in residential care (Sandman et al. 1987).
The origin of this weight loss is not properly understood. It seems to arise from a number of different factors (Gillette-Guyonnet et al. 2000), and the causes may be different depending on the stage of the illness. Loss of autonomy entails difficulties in obtaining food and preparing meals. Behavioural disorders are liable to be accompanied by reduced food intakes. Atrophy of the mesio-temporal lobe could be accompanied by a loss of appetite and changes in eating habits (Grundman et al. 1996). Weight regulation disorders due to damage to the endocrine regulation system, controlled by the hypothalamus, has also been mentioned, as have biological disorders relating to neuropeptide Y, cytokines and cholecystokinin. Finally, in certain cases, it may be due to greater energy expenditure because of increased physical activity (wandering, agitation). However, there is no increase in the metabolism at rest (Niskanen et al. 1993, Donaldson et al. 1996, Poehlman et al. 1997). Interestingly, this gradual disease-related weight loss may be limited by cholinesterase inhibitors (Gillette-Guyonnet et al. 2006). Furthermore, patients suffering from AD are likely to present rapid weight loss in conjunction with an inflammatory syndrome, an acute medical episode, hospitalisation or arrival in a residential care facility (Guérin et al. 2005).

This weight loss may evolve to become protein-energy undernutrition with the consequences this engenders, thus worsening the prognosis of the disease. More specifically, with AD, weight loss is accompanied by an exacerbation of cognitive disorders and an increased risk of mortality (White et al. 1998). Furthermore, in patients suffering from AD living at home, the MNA^{TM} score is an independent risk factor for placement in a care facility (Andrieu et al. 2001).

3.1.2. Nutritional interventions

In certain patients suffering from AD, oral nutritional support has proved its effectiveness on the improvement of nutritional status. A nutritional education programme conducted for one year with care workers caring for AD patients living at home, led to significant improvements in the patients' weights (Rivière et al. 2001). Several clinical studies relating to the administration of oral nutritional supplements have shown a favourable effect on amounts ingested, weight, various anthropometric measurements and micronutrient status (Carver & Dobson 1995, Wouter-Wesseling et al. 2002, Faxen-Irving et al. 2002, Gil Gregorio et al. 2003, Lauque et al. 2004, Young et al. 2004, Salas-Salvado et al. 2005, Wouter-Wesseling et al. 2006). Likewise, support provided by a dietician and high-calorie menus resulted in weight gain in patients suffering from AD (Keller et al. 2003).

However, the effects of this nutritional support on cognitive functions, functional status, the occurrence of complications and mortality have not been studied to the same extent. Only the study relating to the nutritional education programme for care workers showed that cognitive status (assessed by the Mini Mental Score) deteriorated less over a period of one year for patients in the intervention group than those in the control group (Rivière et al. 2001). Other nutritional intervention studies do not show any significant effect on cognitive performance, functional status, risk of hospitalisation or mortality (Faxen-Irving et al. 2002, Gil Gregorio et al. 2003, Keller 2003, Lauque et al. 2004, Salas-Salvado et al. 2005).

In the case of undernutrition, oral nutritional support is a priority and therefore often seems to be effective in improving nutritional status. Should oral nutritional support fail, severe anorexia, especially in cases of rapid weight loss resulting from a medical or psychosocial event occurring in patients suffering from mild or moderate AD, the question of temporary enteral feeding arises, with the aim of recovering a previous nutritional state. No clinical studies have been conducted for this specific indication.

Finally for patients suffering from severe AD, long-term enteral nutrition appears to be of very limited interest. Although there is no randomised study comparing oral to enteral nutrition for patients suffering from AD, a review of the literature suggests that enteral feeding does not limit the risk of breathing pneumopathies, other infections, pressure sores or mortality, nor does it improve functional autonomy or comfort (Finucane et al. 1999). Twenty-three patients with gastrostomies were compared to 18 other patients whose families had refused artificial feeding: there was no difference in the length of survival between the two groups (Murphy et al. 2003). The presence of a nasogastric tube was an independent risk factor for mortality in 67 elderly patients suffering from AD and living at home (Alvarez-Fernandez et al. 2005). All in all, enteral feeding is not recommended for patients suffering from severe AD (Volkert et al. 2006, Gillette-Guyonnet et al. 2006). However, the literature shows a wide diversity in the practices for using enteral feeding in cases of severe dementia, which can be explained by socio-cultural and religious factors (Mitchell et al. 2003, Braun et al. 2005, Clarfield et al. 2006). The decision to begin enteral feeding or not for a patient suffering from severe AD is based on a range of medical and ethical considerations (Gillick 2000, Somogyi-Zalud et al. 2001, Wilmot et al. 2002, Niv & Abuksis 2002, Cervo et al. 2006, Dennehy 2006); multidisciplinary discussions should be held when making such a decision, and any anticipated directives as well as the feelings of the family circle should be taken into account.

3.1.3. Micronutrients

Patients suffering from AD are likely to present a variety of deficiencies, and even a serious deficiency in micronutrients, particularly in group B vitamins, but also in vitamin C, vitamin E, vitamin A, retinol and carotenoids (Sneath et al. 1973, Karnaze & Carmel 1987, Zaman et al. 1992). These observations raise the question of the role of such nutritional deficiencies in physiopathologies and the exacerbation of cognitive disorders. However, dementia may itself be the cause of nutritional deficiencies due to related anorexia and eating disorders.

The intervention studies deal mainly with the administration of vitamins B_{12}, B_9 and B_6. In most cases, a large number of psychometric tests were conducted, before and after the administration of vitamins, and the type of cognitive performance liable to be improved is variable. In small groups of elderly subjects suffering from cognitive disorders or AD associated with deficiencies and severe deficiencies of vitamin B_{12}, two studies regarding the administration of vitamin B_{12} for 6 months reported an improvement in cognitive performance (Martin et al. 1992, Eastley et al. 2000) while two other studies were negative (Carmel et al. 1995, Teunisse et al. 1996). In 96 elderly subjects suffering from dementia, the administration of folates for 2 months improved short-term memory (Passeri et al. 1993). These studies suggest a possible effect of the administration of vitamins B_{12}, B_6 or folates on cognitive performance, perhaps especially for patients with serious deficiencies and suffering from moderate or recent cognitive disorders.

With respect to antioxidant micronutrients, a double-blind placebo-controlled trial was conducted to examine the effect of the administration of alpha-tocopherol, selegiline (for its antioxidant properties) or both compounds, for two years, to a population of 341 patients suffering from a moderate form of Alzheimer's Disease (Sano et al. 1997). The main judgement criteria were the time lapse before deterioration to a severe form of the disease, loss of autonomy, being taken into residential care and mortality. After adjustment for the severity of cognitive disorders, the results showed that the administration of alpha-tocopherol, selegiline or a combination of the two compounds, was clearly linked to an increased period free of these events. However, the methodological quality of this work was later criticised (Pincus 1997). It is therefore an avenue of research to be developed.

In conclusion:
The data provided by the literature does not enable specific nutritional references to be set for elderly subjects with Alzheimer's Disease who do not suffer from undernutrition; their nutritional requirements in terms of macro and micronutrients are very probably covered by the French Population Reference Intakes (ANCs) for healthy elderly people.
In the event of weight loss, a situation which is common in Alzheimer's Disease, oral nutritional support is recommended. This nutritional support is not specific, but must take into account the level of physical activity, which can be significant when behavioural disorders such as agitation and wandering are present. Likewise, deficiencies in micronutrients must be corrected. Finally, enteral nutrition must be considered if rapid weight loss should result from an intercurrent event which is resistant to oral support. In the event of gradual undernutrition resulting from the terminal phase of the disease, enteral nutrition is not recommended.

3.2. Pressure sores

3.2.1. Physiopathology

A pressure sore is defined as tissue damage of ischemic origin, caused by compression of subcutaneous tissue between bony areas and a pressure point. The most frequent sites of pressure sores are the heels, sacrum, ischia and trochanters. In addition to pain and a poor body image, pressure sores are associated with longer hospitalisation and mortality. Although the role of undernutrition in the development of pressure sores is complex, they occur more frequently in malnourished patients (Berlowitz & Wilking 1989, Ek et al. 1991, Bergström & Braden 1992, Reed et al. 2003). This chapter does not deal with the multiple risk factors for pressure sores but provides a basis for possible nutritional intervention.

3.2.2. Prevention of pressure sores

An increase in oral nutritional intake seems to be effective in reducing the incidence of pressure sores. In a population of 672 hospitalised elderly patients, the administration of oral nutritional supplements resulted in a reduction in the number of new pressure sores; however it is difficult to provide a precise level of energy and protein intake (Bourdel-Marchasson et al. 2000). A recent meta-analysis of 15 trials, 8 of which were controlled and randomised, showed a 26%

reduction in the number of pressure sores due to the administration of oral nutritional supplements (Stratton et al. 2005).

3.2.3. Nutritional support for established pressure sores

As part of the treatment of established pressure sores, it is very difficult to distinguish what is attributable to calories, protein and micronutrients: most often, these all vary at the same time. Sufficient energy intake is necessary for a positive nitrogen balance.

3.2.3.1. Energy intakes

The energy requirements of patients with pressure sores were assessed based on the measurement of energy expenditure at rest over 24 hours. This assumes that the physical activity factor, which multiplies the energy expenditure at rest is known, in order to find the 24-hour energy requirement. This cannot be accurately ascertained in the absence of a measurement of energy expenditure over a 24 hour period. A conservative estimate of this factor is between 1.3 (the strict minimum requirement for 24 hours) and 1.5 (taking into account the requirements for substrate renewal, healing and a minimum of physical activity). Furthermore, although the measurements of energy expenditure are accurate from a methodological point of view, they only show the expenditure in the context of a patient with a given pathology and its consequences. In fact – and this is especially true for dietary restrictions – there is an adjustment for the reduced energy expenditure. Thus the measurement for a patient with a restricted diet provides information on the adjusted energy expenditure, which is precisely what leads to the development of pressure sores. So it is a question of minimum energy intake. Real progress will be made when clinical trials are performed that test several energy rations along with the analysis of "hard" criteria such as the prevention of pressure sores or the speed of healing. Another difficulty arises from the very great variability of the characteristics of patients with pressure sores (various pathologies, variable physiological and nutritional conditions and great variations in supplementation). The findings of published trials may therefore appear disappointing and somewhat insubstantial.

In younger patients with neurological deficiencies and pressure sores, three studies have measured energy expenditure at rest and shown that it was high. Liu (Liu et al. 1996) reports energy expenditure at rest of 24.3 kcal/kg/day for young tetraplegic patients with pressure sores, 7.5% higher than that of control patients (22.6 kcal/kg/day), and 16% higher than that of tetraplegic patients without pressure sores (20.9 kcal/kg/day). In Alexander's study (Alexander et al. 1995), the energy expenditure at rest linked to the presence of pressure sores is 21% higher (25.9 compared to 21.4 kcal/kg/day) for paraplegic patients. Lastly, this difference is 21% in Aquilani's study, which was also conducted on paraplegic patients (Aquilani et al. 2001). Therefore in younger subjects, energy requirements at rest in the presence of pressure sores vary from 25-30 kcal/kg/day (20) to 27-32 (a 7.5% increase) or even 30–38 kcal/kg/day (up 20%).

For ailing elderly subjects, there is only one study (Dambach et al. 2005) comparing energy expenditure at rest in patients with pressure sores to that of control patients matched for their Norton score. This study shows firstly that Harris and Benedict's equation (1919) enables the energy expenditure at rest for elderly people with pressure sores to be determined with sufficient accuracy. There is therefore no need to measure energy expenditure. Furthermore, the energy expenditure is 5% higher (non-significantly, 20.7 compared to 19.6 kcal/kg/day) in patients with pressure sores than in patients without pressure sores. This study also shows that the size and surface area of the pressure sore, or its stage, do not affect energy expenditure at rest.

Apart from these studies in which energy expenditure was measured, many expert opinions recommend 30-35 kcal/kg/day (Thomas 1997 and 2001, European Pressure Ulcer Advisory Panel (EPUAP) 2003), or even 40-50 kcal/kg/day (Lesourd 1997). Whatever the case, it would appear that increased energy expenditure is not sufficient to improve the speed of healing (Mathus Vliegen 2004). There is currently no consensus on the intake, although this should doubtless be above 30 kcal/kg/day.

3.2.3.2. Protein intakes

The same methodological comments are valid for protein requirements as no study has analysed these in this population using validated tools.

Although the experimental patterns of the clinical studies are not optimal (few randomised placebo-controlled trials), it appears than an increased protein intake (24% of calories in the form of proteins, i.e. 2.1g/kg/day, compared to an intake of 14% of calories in the form of proteins, i.e. 1.4g/kg/day) increases the speed of healing (Breslow et al. 1993).
It seems that the recommended protein intake for healthy elderly people (0.8 - 1g/kg/day) is not sufficient. An intake of 1.5g/kg/day may reasonably be recommended (Thomas 1997 and 2001, EPUAP 2003).

With respect to amino acids, the administration of glutamine, a fundamental substrate for the functions of enterocytes and the immune system, has not shown any beneficial effects on healing. The same is true for branched-chain amino acids. Other amino acids with functional properties (properties other than the calorie intake they represent), such as ornithine alpha-ketoglutarate, have shown confirmed benefits for burn patients, in plastic surgery and amputation (Cardenas et al. 2002). In these cases healing occurs more quickly. Four randomised studies versus an isocaloric placebo, versus an isonitrogenous intake or versus usual care tested the effectiveness of this compound in patients with pressure sores, after six to eight weeks of treatment at 10g/day. Although the methodological quality of these trials is poor, the results are consistent and suggest that after 6 weeks, healing occurs faster in the groups receiving ornithine alpha-ketoglutarate supplements than in the control groups (Meaume & Piette 1997). Only one clinical trial, with 16 patients aged 37 - 92 years, suggests that an oral nutritional supplement enriched with arginine, vitamin C and zinc promoted improved healing, as measured by the PUSH score (Pressure Ulcer Scale of Healing, which measures the surface area and depth of the wound, the quantity of exudate and the type of tissue) (Desneves et al. 2005). The other studies related to specific nutritional supplements intended to boost healing have not been controlled or do not provide statistical analysis (Benati et al. 2001, Soriano 2004).

3.2.3.3. Micronutrients

Although intakes of zinc and vitamins A and C are a logical prescription for improving healing, no study has been conducted as to the requirements for these nutrients. There is little proof of the effectiveness of administering micronutrients. Administration of vitamin C at a dose of 1g per day has not shown any benefit in terms of healing of pressure sores compared to a dose of 20mg/day (Ter Riet et al. 1995). Zinc has been recommended for some ten years now, without any proof of its effectiveness. The same is true for vitamin A and iron. With respect to oral nutritional supplements of micronutrients, once again only one clinical trial (+ arginine, vitamin C and zinc) suggests that they could speed up healing, without it being possible to attribute this effect to arginine or the other two micronutrients (Desneves et al. 2005). The other studies (+ vitamin C, zinc and vitamin E), have not been controlled or do not provide statistical analysis (Benati et al. 2001, Soriano 2004). It is likely that these micronutrients are useful if a deficiency is found. Multiple supplement strategies may be of interest (Brown 2004).

In conclusion:
Elderly people with pressure sores are usually undernourished. The minimum energy intake is probably 30 kcal/kg/day, but the levels to be achieved to correct undernutrition and promote healing are probably somewhere between 30 and 40 kcal/kg/day; this has not yet been validated. For the time being there are few arguments in support of very high intakes, above 40 kcal/kg/day.
Likewise, a protein intake of 1.5g/kg/day may be recommended. Amino acids with functional properties in addition to nutritional support (ornithine alpha-ketoglutarate) are probably beneficial.
Deficiencies and severe deficiencies in micronutrients must be corrected but supranutritional intakes have not proved to be of interest when requirements are covered. Other studies are

necessary to ascertain the ideal energy and protein intakes in the treatment and prevention of pressure sores.

3.3. Hip fractures

Hip fractures are one of the most serious traumatic injuries which can occur in frail elderly people. Nutritional status is one of the parameters explaining the occurrence of this type of fracture and its seriousness in terms of mortality, morbidity, risk of loss of autonomy and cost of care.

3.3.1. Epidemiology of hip fractures

In 2004, 50,000-55,000 elderly people in France over 65 suffered from a fracture of the hip. The incidence of hip fractures increases exponentially with age (Baudoin 1997). The incidence of hip fractures is 8/1000 after age 80, with twice as many women as men. The average age at the time of fracture is 81 for women and 73 for men. This increase in the risk of fracture with age results from reduced bone resistance and frequent falls (Dargent-Molina et al. 1996). Swedish trend forecasts for 2010 appear to show an overall increase in hip fractures in men irrespective of the fracture site and a slight decrease in women (Lofman et al. 2002).

The annual cost for the hospitalisation and physiotherapy needed to treat hip fractures is estimated at some €610 million (Baudoin 1997).

3.3.2. Prognosis for hip fractures

The occurrence of hip fractures is responsible for increased morbidity and mortality in elderly people. The mortality rate following a hip fracture is high - 11% in the first three months and 37% during the first year after the operation, and all the higher for elderly and frail patients (Lyons 1997). This rate reaches 48% for men having suffered a hip fracture after the second year. The relative risk factor for mortality at 6 months is 3 [CI 95%: 1.9-4.7) and goes down to 1.9 CI 95%:1.6-2.2) after that point (Empana et al. 2005). This data has been disputed in a recent study (Richmond et al. 2003) showing that on the contrary the population of over-85-year-olds has a lower risk of mortality than the 65–84 year-old population after 12 and 24 months of follow-up care. The American Society of Anesthesiology (A.S.A.) Classification appears to be a good tool for predicting survival over this period.

3.3.3. The role of undernutrition in hip fractures

Protein-energy undernutrition is liable to play a part in the occurrence of hip fractures. Investigations in English-speaking countries have shown that one fracture patient in two ate less than half of the ANCs or was suffering from established undernutrition (Dickerson 1979). Other studies (Lumbers et al. 2001) have also shown that one third of elderly people suffering from hip fractures did not have their protein requirements covered.

There is a very close link between hip fractures and undernutrition. Protein-energy undernutrition contributes to the risk of loss of muscle strength, loss of pelvic fat layers that provide protection against falling and loss of cortical bone mass in the hip (Vellas et al. 1992, Bonjour et al. 1996). It has been demonstrated that involuntary weight loss is an independent factor for predicting a fracture event (for each loss of 10% of body weight, the relative risk factor is 1.81 [CI 95%: 1.26-2.61] (Ensrud et al. 1997). Furthermore, low protein intakes are associated with the risk of fracture (Hannan et al. 2000).
Plasma concentrations of IGF-1, an anabolic hormone, is low in patient populations suffering from hip fractures (Bachrach-Lindström et al. 2001) and increasing protein intakes following a hip fracture increases IGF-1 levels and reduces contralateral bone loss after the fracture (Schurch et al. 1998). The concomitant loss of fatty mass reduces the physical protection of the bone.

Furthermore, undernutrition plays a role in the appearance of osteoporosis due to reduced calcium intake. Calcium intake is reduced on average by around 600 - 800mg/day in elderly people, whilst the Dietary Reference Intake in France is 1200mg/day (Cynober et al. 2000). Along with this insufficient quantity of calcium ingested, reduced exposure to the sun through being housebound or in residential care results in hypovitaminosis D and secondary hyperparathyroidism due to chronic hypocalcemia (Nieves 2005) which tends to make the hip, already affected by age-related osteopenia and deprivation of anabolic male and female sex hormones, even more frail. This secondary hyperparathyroidism is a powerful factor in the prediction of a first fall independently of plasma vitamin D levels (Sambrook et al. 2004, Pasco et al. 2004). In housebound elderly people, a low intake of the nutrients required for muscle and bone metabolism (calcium, vitamin D, magnesium and phosphorus) is associated with a greater incapacity of the lower limbs, as measured by functional tests (Sharkey et al. 2003).

Finally, undernutrition worsens the post-operative prognosis of elderly people with hip fractures. A primary study (Bastow et al. 1983) showed that a reduced arm circumference (muscle mass) and skinfold thickness (fatty mass) were associated with low survival rates after hip fractures.

Furthermore, the surgical intervention for hip fractures and the ensuing prolonged hospitalisation worsens the nutritional status of elderly people. Variable-length pre- and post-operative fasting periods are a factor in increased energy deficit. Inflammatory stress also occurs almost immediately following the fracture event, as shown by CRP measurements which may exceed 100mg/l and remain high for 2-4 weeks after the operation. This inflammatory stress is found on admission to follow-up care and physiotherapy and is a cause of anorexia due to the synthesis of proinflammatory cytokines (IL-6 and TNFα). All of these events constitute a series of risks for energy deficit, which only serve to exacerbate an already poor nutritional status (Paillaud et al. 2000).

3.3.4. Energy requirements

Energy requirements can be determined by techniques for measuring energy expenditure. They can also be measured by analysing the impact in intervention studies increasing the overall share of calories supplied by macronutrient or protein intakes on nutritional status and follow-up care after an operation on a fracture.

The study of Jallut et al. (1990) on a selected population with hip fractures shows an average base metabolism of 1283 ± 194 kcal/day compared to average calorie values ingested of 1097 ± 333 kcal/day. In the study by Paillaud et al. (2000) the basic energy expenditure on admission to follow-up care after a hip fracture is 4.9 ± 0.4 MJ/day (1170 kcal or 31 - 34 kcal/kg of muscle mass/day) irrespective of nutritional status. These basic metabolism values are higher than those found by Camillo et al. (1992) (22.1 ± 0.7 kcal/kg where the BMI > 20 *vs* 28.4 ± 1.3 kcal/kg where the BMI < 20) but the population studied is not fully comparable; this study examined both elderly people having been operated on for a bone fracture and patients having undergone digestive surgery with a colostomy. The same observations are reported in the work of the DEPAM group (Alix et al. 2007): for elderly patients in short stay hospitalisation and follow-up care, 20% of whom had a fracture of some nature, energy expenditure at rest varies between 19 ± 2 kcal/kg/day for a BMI > 21, and 21 ± 2 kcal/kg/day for lower BMIs. Therefore the increase in basic energy requirements mainly affects the population of undernourished patients. Total energy expenditure, with a correction factor of 1.5, may therefore be approximately 30 kcal/kg/day. The intake needed to achieve sufficient rehabilitation, healing or clinical improvements to enable the patient to return home is very probably higher than the requirements estimated to simply maintain metabolic balance.

There are a greater number of intervention studies immediately following surgery or some time later, after time spent in a physiotherapy unit, but their methodological soundness is variable. A review of the literature published in 2006 (Avenel & Handoll 2006) analysed the results of oral protein-energy supplementation, presence or absence of exclusive enteral feeding, protein supplements, vitamin supplements or ornithine α-ketoglutarate versus peptide supplements. Intervention studies have been conducted on elderly patients selected on the basis of their nutritional status. It is difficult to compare these due to incomplete or unknown data with respect to comorbidity and related treatments, the composition of calorie and protein supplements, the length of the intervention, the overall amount of calories ingested and patient compliance, basic anthropometric data and how it is monitored, quality of life and its fluctuations. Furthermore, the main parameter for assessing the impact of the intervention is often different from one study to another. Thus, the two primary studies using calorie supplementation (254 kcal/day), Delmi et al. (1990), or protein supplementation of 20.4 g/day (supplements with or without proteins), Tkatch et al. (1992), in a short-stay surgery ward and physiotherapy unit respectively, seem to show improvements in terms of survival, functional recovery and cost. However, with other assessment criteria such as the length of hospitalisation or mortality rate, the results of recent studies do not appear to be convincing (Avenel & Handoll 2006). Nonetheless a non-significant trend towards reduced complications and a significant reduction of "unfavourable developments" combining complications and mortality (Delmi et al. 1990, Stabelforth 1986) can be noted. After the age of 80, protein-calorie supplementation is difficult to carry out over an extended period of time due to lack of compliance resulting from the lack of attractiveness of the products on offer (Lawson et al. 2000). The studies testing enteral feeding do not show any gain in terms of morbidity and mortality, functional gain or reduced costs, either because the length of enteral feeding was too short to enable any benefit, or because the respiratory complications of this technique work against it.

Opinions therefore seem to concur that at least one in two elderly people suffering from hip fractures are already undernourished. Surgical intervention, hospitalisation, pain and treatment are likely to worsen their nutritional status. Physiotherapy increases energy requirements. Nutritional support is recommended, without it being possible to determine with great accuracy the protein and calorie levels to be achieved (at least 30 kcal/kg/day and perhaps as much as 40 kcal/kg/day).

3.3.5. Protein requirements

The protein requirements for patients with hip fractures are not known. The average increase in protein intakes in supplementation studies is estimated at 20 g/day, in addition to spontaneous intakes (Avenel & Handoll 2006). However, spontaneous intakes of calories and protein are not known. The result of these interventions on complications, length of hospitalisation and functional recovery tends to be favourable, but is not significant due to the groups being too small or poor supplementation compliance when supplements are administered over an extended period. However, due to the fact that elderly people with hip fractures are usually undernourished, we suggest that protein intakes should exceed the Dietary Reference Intake for elderly people in good health, with 1.2 - 1.5 g/kg/day.

3.3.6. Micronutrients

3.3.6.1. Vitamin D and Calcium

The administration of vitamin D and calcium to elderly people living in care homes significantly reduces the number of fractures of the femoral neck, as compared to a control group, even though there is insufficient knowledge of the optimal doses of vitamin D and calcium and how they work (Chapuy et al. 1992 et 2002, Harwood et al. 2004). A randomised double-blind study combining 1g/day of calcium and 100,000 UI of vitamin D once every 4 months showed a reduction in the number of fractures of around 20% for a monitoring period of 5 years for 65-85 year-olds living at home (Trivedi et al. 2003). A recent Swedish study does not confirm the link between the consumption of calcium and vitamin D and the risk of hip fracture (Michaelsson et al. 2003). At mid-term, the study by Feskanich (Feskanich et al. 2003) shows a 37% reduction in the risk of hip fracture with daily intakes of 12.5 µg/day of vitamin D, but no preventive effect of intakes of calcium or dairy products. No study of this type has been conducted with frail elderly people. The effectiveness of calcium and vitamin D supplementation on the prevention of vertebral and non-vertebral fractures is therefore a subject of debate (Nieves 2005). Most often, the negative studies relate to subjects with normal vitamin D plasma levels, no related calcium supplementation or the administration of lower doses of vitamin D (400 UI/j).
A meta-analysis of trials on the effect of calcium and vitamin D supplementation on falls shows that with a minimum calcium intake of 500mg/day and a vitamin D intake above 600 UI/day, the number of falls is reduced by 22%. One fall will be avoided for every 15 people treated (Bischoff-Ferrari 2004).

Once the fracture has occurred, no change to oral vitamin D intakes seems to be effective in improving the functional prognosis (Harwood et al. 2004). Finally, the administration of calcium and/or vitamin D does not reduce the incidence of fractures in subjects who have already had a hip fracture or those who have a high risk of fracture (Porthouse et al. 2005, Grant et al. 2005).

The vitamin D and calcium intakes to be recommended do not therefore appear to be different from the ANCs for elderly people over 75 (10-15 µg/day of vitamin D and 1.2 g/day of calcium). It must therefore be ensured that these intake levels are reached for all elderly people, in particular elderly people in residential care, and supplementation offered if necessary.

3.3.6.2. Vitamin K

Women with the highest intakes of vitamin K (quintiles 2-5) have a lower risk of hip fracture (RR: 0.70; 95% CI: 0.53, 0.93) than those with the lowest intakes (quintile 1: < 109 µg/day) (Feskanich et al. 1999). The study by Booth (Booth et al. 2003) on the Framingham cohort shows a significant link between the consumption of vitamin K (lower quartile versus upper quartile) and the mineral bone density of the neck of the femur and vertebrae in women, but not in men. In spite of these observations, there are no intervention studies that recommend an increase in daily vitamin K as a preventive measure or additional treatment for hip fractures.

3.3.6.3. Vitamin A

Serum vitamin A levels do not reflect the organism's reserves very faithfully. A study on a NHANES I cohort shows a link between plasma vitamin A concentrations and the risk of fracture in the form of a U curve, the risk increasing for the lower and upper quintiles (RR respectively of 1.9 (95% CI: 1.1 - 3.3 and 2.1 95% CI: 1.2 - 3.6)) (Opotowsky et al. 2004). However the risk of a vitamin overdose is greater than the risk of deprivation in First World countries. There is no need to alter ANCs to prevent or treat hip fractures.

3.3.6.4. Micronutrient combinations

There is no proof that intakes of micronutrient-enriched solutions in isolation can improve the nutritional status and the prognosis of patients suffering from hip fractures. The only study assessing this type of preparation is that of Delmi (Delmi et al. 1990) but the effect of the combined calorie and protein-enriched diet is cannot be dissociated from the possible effects of the micronutrients added to it.

In conclusion:
Deterioration in nutritional status precedes and promotes the occurrence of hip fractures. In this respect, hip fractures are a sign of frailty in elderly people. Furthermore, nutritional status deteriorates following a hip fracture and is a major prognostic factor.
The data provided by the literature does not allow precise nutritional references to be suggested, but an increase in protein and calorie intakes should enable the prognosis of these patients, who are often undernourished, to improve. An increase in nutritional intakes to 30 – 40 kcal/kg/day and 1.2 - 1.5 g/kg/day of protein is suggested.
The amounts of vitamin D and calcium to be recommended appear to be the same as those recommended for elderly people over 75 (10 - 15 µg/day of vitamin D and 1.2 g/day of calcium) as part of the ANCs.

3.4. Bronchopulmonary and urinary infections

The frequency and seriousness of infectious diseases increase with age. Elderly people often suffer from bronchopulmonary and urinary infections. There are many different, complex reasons for this increased susceptibility to infection, and the related multiple chronic illnesses, loss of autonomy, immunosuppressive treatments and repeated hospitalisations are all additional factors which may explain the increased number of infections in elderly people.

Undernutrition plays a role in weakening the immune system and the occurrence of infections. The extent of its actual role in immune malfunction in elderly subjects is the subject of debate.

3.4.1. Pneumopathies in elderly subjects: epidemiology and risk factors

The incidence of community-acquired pneumopathies increases with age. In a Finnish study, among 46,979 inhabitants, the incidence of community-acquired pneumonia in the population of over 75 year-olds was almost six times higher than that in the population of 15-59 year-olds (Jokinen et al. 1993). Elderly people living in care homes were particularly vulnerable (Mylotte 2002). This acute pathology is responsible for a high rate of mortality in elderly people. The micro-organisms found in this population are rarely different from those found in pneumonias in young adults, but with a higher proportion of cases due to *H. influenzae*, *S. aureus*, and gram-negative bacteria (Marrie 2000). It is difficult to distinguish viral pneumopathies from those of bacterial origin; the two most frequent viruses are the Respiratory syncytial virus and Influenza A virus (Falsey et al. 1995).

The identified risk factors for community-acquired pneumopathies in elderly people living at home or in care homes are loss of autonomy, absence of influenza vaccination, presence of a nasogastric tube, alcoholism, swallowing difficulties, low albuminemia, chronic broncho-pneumopathy, tracheostomy, very old age and subclinical inhalations detected by videofluoroscopy in particular during cerebrovascular accidents or in Alzheimer's Disease (Marrie 2000, Mylotte 2002).

3.4.2. Urinary infections: epidemiology and risk factors

The incidence of urinary infections increases with age and is particularly high in geriatric wards. Most infections are so-called asymptomatic bacterial infections which are not accompanied by any clinical signs of infection and require no treatment (Nicolle et al. 2005). Symptomatic bacterial infections in elderly subjects, however, play a role in the comorbidity of elderly people and require antibiotic medical treatment. In a European prospective study conducted in 141 hospitals in 25 European countries, there were a total of 298 urinary infections occurring on the day of the study, representing an incidence of 3.55 episodes/1000 patient days and an estimated prevalence of 10.65/1000 (Bouza et al. 2001). *Escherichia coli*. is the main bacterium responsible for these urinary infections, regardless of their site of occurrence.
The main factors contributing to these high rates of bacterial infections are loss of autonomy, chronic neurodegenerative diseases with bladder malfunction, urinary and fecal incontinence, urinary catheterisation, hypertrophy of the prostate in men and atrophy of the genital mucosa in women (Nicolle et al. 2005).

3.4.3. Interactions between infections and undernutrition in elderly people

The immune system deteriorates with age. This immune dysfunction is called immunosenescence and prevails over adaptive immunity. It contributes to the increased vulnerability of elderly people to infections. This increased vulnerability to infections includes the inability to react to new infectious germs, resulting in more frequent and more serious occurrences of various infections, in addition to the reactivation of latent viruses and by extension decreased effectiveness of vaccines. The role of undernutrition of elderly people in the occurrence of one or several immune system anomalies has not been fully established (High 2001).

3.4.3.1. Principle age-related anomalies of the immune system

The immune system is divided arbitrarily into two components; the natural innate immune response and the acquired adaptive immune response. Its main dysfunctions are described below.

In the absence of a related pathology, the innate immune response (activation of the complement system, phagocytosis, NK cells) is not markedly affected by age. However, ageing is associated with significant deterioration of the adaptive immune response. The main changes are characterised by a decrease in thymic hormones, an increase in memory T cells and a reciprocal decrease in naive T cells both in the TCD4 and TCD8 population, and reduced function of T cells. Furthermore, humoral response, both by the B cells produced in the hematopoietic marrow (Castle 2000) and by the follicular dendritic cells in the germinative centre, show age-related deterioration.

3.4.3.2. The role of undernutrition in immunosenescence

The role of undernutrition in elderly people in the occurrence or exacerbation of one or several anomalies of the immune system is not yet fully understood. Age-related deterioration of the immune system (described above) depends on the state of health of the elderly individual and the presence of related chronic pathologies. These changes are less significant in elderly people in excellent health and are selected according to criteria which excludes any elderly person with a related chronic pathology, an anomaly in their biological tests or taking medication (Ligthart et al. 1984). Conversely, they are accentuated in undernourished elderly people or elderly people with micronutrient deficiencies (Mazari 1998, Walrand 2001).

3.4.3.3. Association of undernutrition with infectious pathologies

A few studies on the risk factors for nosocomial infections have examined the role of undernutrition in the occurrence of these infections (Harkness et al. 1990, Hussain et al. 1996, Trivalle et al. 1998, Bourdel-Marchasson et al. 2001, Rothan-Tondeur et al. 2003). The nutritional criteria used most frequently in these studies were weight, Body Mass Index and albuminemia. None of these studies, with a multivariate analysis, has shown that undernutrition was an independent risk factor. However three other studies have examined the nutritional status of elderly people with infections more closely. In 1637 patients with an average age of 61, undernutrition as assessed by the Nutritional Risk Index is an independent risk factor for nosocomial infection (Schneider et al. 2004). In 185 elderly people hospitalised for follow-up care, nutritional status on admission was significantly worse in the two groups of people with one or several nosocomial infections than in the group of patients without nosocomial infections (Paillaud et al. 2005). Finally, a certain number of nutritional parameters (serum levels of proteins, iron and vitamin E) and immunological factors were significantly lower in the group of elderly people that did not respond to the flu vaccine as compared to the group of those that did respond (Fulop et al. 1999).

3.4.4. Nutritional strategies for preventing infections or limiting their severity

In spite of the very large number of studies published in this field, very few are conclusive from a clinical point of view. Most of these intake studies showed an improvement in immune response but without having sought or demonstrated a preventive or positive effect on infectious disease. Furthermore, very few studies have been conducted with hospitalised elderly people or those in residential care.

3.4.4.1. **Protein and calorie requirements**

At the present time, there have been no observation studies to determine daily energy expenditure or protein requirements specifically for elderly people with infections. Many other studies on oral, enteral or parenteral nutritional support have been conducted for various pathologies but none have focused on specific care for infectious pathologies in elderly subjects.
In conclusion, for elderly people with infections, we suggest that the ANCs for healthy elderly subjects should be observed, i.e. a total of 36 kcal/kg/day and 1 g/kg/day of proteins.

3.4.4.2. Micronutrients

Multivitamins

Most multivitamin supplements contain vitamins A, C, E and also B_1, B_2, B_6, B_{12}, vitamin D, minerals (calcium, magnesium) and trace elements such as zinc, selenium, copper, iron and iodine.

In the meta-analysis by El-Kadiki & Sutton (2005), of the 1454 studies analysed, only 6 were correctly conducted from a methodological point of view and only two of these 6 studies examined elderly people in residential care. There is a high degree of variability between the studies in terms of length of monitoring, assessment of the infection and the number of subjects, which limits comparison. Only one study (Chandra 1992) reported a significant difference in the average annual number of days of infection, with a reduction in the group taking multivitamins as compared to the placebo group. With respect to the incidence rate for infections and the occurrence of at least one infection, the meta-analysis of these studies does show a significant difference.

Thus there is no evidence at the present time that an intake of micronutrient solutions in isolation reduces the incidence and number of infectious episodes in elderly people. We do not recommend multivitamin supplements for elderly people to prevent infection or reduce its morbidity.

Antioxidant micronutrients (Se, Zn, Vit C, Vit A and E)
Although some studies have shown that an intake of 200 mg/day or 800 mg/day of vitamin E in healthy, non-undernourished elderly people improves immune response (High et al. 2001), the data relating to the prevention of broncho-pulmonary infections and limiting their severity are incomplete or disputed (Graat et al. 2002).

No study on intakes of vitamin A in elderly people has shown an effect on the incidence of infectious pathologies and their severity (Murphy et al. 1992; Girodon et al. 1997).

There are very few studies relating to the impact of a vitamin C intake on infectious pathologies in ailing elderly subjects. In a study (Hunt et al. 1994) on vitamin C intakes (200 mg/day) in 57 elderly people hospitalised for a broncho-pulmonary infection, Hunt demonstrated that the group receiving the supplement had a more favourable clinical outcome than the placebo group. Conversely, for a large cohort of 725 patients from 24 geriatric wards, a 2-year study by Girodon et al. (1999) of the intake of trace elements (selenium and zinc) or vitamins (vitamins C, E, beta-carotene) or a placebo, using a 2X2 factor approach, did not show a decrease in the number of broncho-pulmonary infections in the vitamin group compared to the placebo group, contrary to the trace elements group.

Two studies on intakes of zinc (20 mg/l) and selenium (100 µg) in elderly people in residential care showed a preventive effect on the occurrence of broncho-pulmonary infections. (Girodon et al. 1997, Girodon et al. 1999). Other nutritional intervention studies with different forms and different dosages of zinc for elderly people have shown improved immune response but have not assessed the clinical impact on the incidence of infections (High et al. 2001).

In conclusion:
Current data provided by the literature does not make it possible to affirm that a modification in nutritional intakes prevents the occurrence of infections in healthy elderly subjects.
There are relatively few studies on the administration of micronutrients to prevent infections in elderly subjects and these do not allow any conclusions to be drawn with respect to their effectiveness. We therefore do not recommend a multivitamin supplement to prevent infections or reduce their morbidity.
Finally, there is no specific data as to the nutritional requirements of elderly individuals suffering from infections; because of this lack, we suggest that the ANCs for the general elderly population be observed.

In summary:
The nutritional status of frail elderly people is particularly critical and nutritional intervention is probably an important means of preventing the deterioration of individuals' state of health, autonomy and quality of life. Attempts to establish specific nutritional references are hindered by the difficulties encountered in providing a universally objective definition of this state of frailty as well as the establishment of nutritional requirements. Most of the data in the literature relates either to elderly populations considered to be in good health or to elderly patients suffering from specific pathologies.
In medically stable, frail elderly people who are not undernourished, the ANCs for the elderly population appear to be a reasonable objective.

In situations of undernutrition, as can be the case with elderly people suffering from Alzheimer's Disease, pressure sores, hip fractures, infections, a whole host of acute pathologies or decompensation of chronic pathologies, it appears justified to suggest higher protein and calorie intakes: 30-40 kcal/kg/day and 1.2–1.5 g/kg/day of proteins.
However, at the present time, no clinical data justifies establishing nutritional references for micronutrients above those set by the ANCs for elderly subjects.

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Key words

Frail elderly people, nutritional references, Alzheimer's disease, pressure sores, hip fracture, bronchopulmonary infections, urinary infections.

The Director General

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