Chapter 26
Healthy Nutrition for Older People

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Abstract The role of nutrition in health has fascinated humans for millennia. Currently, there is a substantial body of research guiding better practices to prevent or treat age-related conditions through nutritional interventions. Chronic degenerative conditions such as cardiovascular disease, sarcopenia and frailty, diabetes, cancer, osteoporosis, prostatic hyperplasia, menopause, age-related macular degeneration and many others, are amenable to nutritional interventions which, in association with specific treatments, may help alleviate the burden of the disease. Nutritional principles can also be applied for the prevention of each condition. In this chapter, there is a presentation regarding some of these principles, mainly focusing on the latest findings in each case. The aim is not to discuss all diets and nutrients suitable for each condition, but rather to use nutrition as a pretext to elucidate some biological mechanisms and processes involved in age-related degeneration. Certain intricacies of chronic degeneration, inflammation, oxidative damage and other age-related processes are at the heart of this discussion, which also examines the action of a number of nutrients or nutritional supplements. It is important to highlight that due to the fact that age-related diseases are multifactorial, it is necessary to employ a multi-pronged approach, tailored to the needs of each patient.

Keywords Health · Ageing · Age-related diseases · Inflammation · Cancer

26.1 Introduction

Chronic degeneration leads to age-related diseases which, in turn, affect the normal function of each one of us. From a clinical perspective, it is important for each individual to be able to live and operate in an environment within the limits imposed by physical, psychological and sociocultural challenges. If one is able to successfully overcome these challenges, then this individual may 'age successfully' and function well, to achieve their life goals. Although there are several elements which may

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S. I. S. Rattan and G. Kaur (eds.), *Nutrition, Food and Diet in Ageing and Longevity*, Healthy Ageing and Longevity 14, https://doi.org/10.1007/978-3-030-83017-5_26

help us overcome successfully these life challenges, this chapter will focus on the nutritional aspects.

Ageing, in other words, 'time-related dysfunction' (Kyriazis 2020), is associated with an increased risk of certain conditions and diseases. Here we will discuss some common ones: osteoarthritis, cardiovascular disease, cancer, age related macular degeneration, menopause, osteoporosis, Parkinson's disease, dementia, sarcopenia and frailty, and benign prostatic hyperplasia. On some occasions, the nutrients discussed here have been used since antiquity for their healthy-sustaining properties. Modern science has attempted to elucidate the exact mechanisms of action, and how these mechanisms may translate into concrete clinical benefits. In addition, many nutrients exhibit hormetic, dose–response benefits, and this presents an opportunity to discuss the increasingly important phenomenon of hormesis (Rattan and Kyriazis 2019). Below is a presentation highlighting certain advantages of nutrients, as these may be used against age-related conditions. The presentation is in no particular order, but aims to be balanced, provides a stimulus for further exploration, and covers most such conditions.

26.2 Osteoarthritis

At the heart of osteoarthritic (OA) changes is chronic inflammation. Therefore, nutritional products which regulate inflammation should provide benefit, both with regards to anatomical changes and clinical symptoms. One example is the case of catechins, chiefly found in green tea. Green tea catechins downregulate several inflammation processes and upregulate anabolic factors (Reddy et al. 2020). It was also shown that catechins can modulate miRNA expression and improve collagen protection (Luk et al. 2020).

In addition to the catechins, the role of dietary fatty acids is increasingly being recognized. In a 16-week randomized, double-blind, placebo-controlled study examining the effects of fish oil (2000 mg/day docosahexaenoic acid plus 400 mg/day eicosapentaenoic acid), it was found that these oils improve the pain of OA in overweight patients (Kuszewski et al. 2020). Supplementation with omega-3 fatty acids is associated with decreased pain and improvement of function, through modulation of apoptosis, reduction of oxidative stress and a decrease in prostaglandin production (Loef et al. 2019). One of the actions of docosahexaenoic acid, i.e. modulation of apoptosis, has been observed in OA cell models (Xu et al. 2019).

Another nutritional agent, which can have some benefit in OA is resveratrol, acting as an anti-inflammatory, anti-oxidative factor. Resveratrol modulates the function of the TLR4/Akt/FoxO1 axis which is involved in inflammation. Specifically, it upregulates phosphoinositide-3-kinase-Akt (PI3K/Akt) phosphorylation, inactivates FoxO1, and reduces Toll-like receptor 4 (TLR4) and inflammation activity (Xu et al. 2020). In a model of temporomandibular osteoarthritis, treatment with resveratrol was found to be associated with prevention of inflammation, reduction of chondrocyte apoptosis, and overall reduction of cartilage destruction (Yuce et al.

2020). Resveratrol is widely considered as having several beneficial actions in many conditions, and it will be discussed again later.

Other nutritional agents which were found to benefit OA:

- Ginger (through inhibition of prostaglandins, acting as an agonist of vanilloid nociceptor, and as antioxidation agent) (Rondanelli et al. 2020).
- Garcinia mangostana (a sweet, juicy tropical fruit) by targeting and suppressing pro-inflammatory cytokines (such as IL-6, TNF-α, and INF- γ) and other factors (NF-κB, STAT3, and COX-2) (Chiu et al. 2020). Extracts of this fruit could also be beneficial in other conditions where inflammation plays a role (Tsai et al. 2020).
- Vitamin K. There are two types of this vitamin, namely vitamin K1 (phylloquinone) and vitamin K2 (a series of menaquinones) with some differences in properties. Vitamin K is known to be associated with modulation of chronic inflammation and it can thus be of benefit, as a dietary supplement, in OA as well as in several other age-related conditions (Simes et al. 2020). Vitamin K1 is found mostly in green leafy vegetables (kale, spinach, lettuce, Swiss chard). Vitamin K2 is in meat, dairy products, liver, eggs, and Japanese "natto," (fermented soy beans).

26.3 Cardiovascular Disease

The nutritional approach into prevention and treatment of cardiovascular disease in older people is wide-ranging. Here, the discussion will revolve around only certain aspects of this approach, presenting the latest research with regards to only a few nutritional factors.

One relevant such factor is vitamin E, which reduces oxidative stress and inflammation during cardiovascular events. Studies show that vitamin E deficiency is associated with an increased risk of cardiovascular events, although studies of vitamin E supplementation in such events have not been definitive (Ziegler et al. 2020). It may be the case that acute supplementation during myocardial infarction will yield better results than chronic preventative consumption through the diet.

Another nutrient which plays a huge role in cardiovascular disease is the group of omega-3 fatty acids already mentioned above. The role of omega-3 fatty acids (such as eicosapentaenoic acid, and docosahexaenoic acid) is well recognized in reducing inflammatory mediators (cytokines and leukotrienes) and atherosclerosis. One of the mechanisms involved is reprogramming of triglyceride-rich lipoproteins (TRLs) (Shibabaw 2020).

Studies of marine omega-3 fatty acids (1 g/d) and vitamin D3 (2000 IU/d) in 25 871 men aged over 50 and in women aged over 55 years for five years, did not find significant benefits of vitamin D with regards to cardiovascular events, although there was a reduction of total coronary risk from the marine fatty acids (Manson et al. 2020). But, as vitamin D can be of benefit in other age-related conditions (for instance osteoporosis), its role remains important. Nevertheless, omega-3 fatty acids are being proven consistently beneficial in reducing the risk of cardiovascular disease.

An important subject that should be mentioned here is that of Calorie Restriction, including the practice of Intermittent Fasting. This notion is crucial in ageing, and can provide information regarding all age-related degenerative conditions. However, it is something that can be practically difficult or impossible to apply on humans as a daily practice. During a calorie restricted diet, the subject is fed approximately 30% (or other proportions) of the normal *ad libidum* diet, and this has been shown to have a host of positive (as well as negative) effects on the organism. The effects are evident when the total amount of calories is restricted, regardless of the diet composition (Brandhorst and Longo 2019). Due to the fact that a routine calorie restricted diet cannot be applied on an average human (due to practical restrictions, hunger and other adverse effects), another pattern that can be of use is intermittent fasting. A short-term 'fasting-mimicking' dietary approach is a periodic, low-calorie, and low-protein dietary approach which can have the beneficial effects without the adverse effects of a chronic and continuing calorie restricted diet (Crupi et al. 2020).

In more general terms, and leaving the subject of calorie restriction aside, adherence to a healthy dietary pattern is as significant as the contents of such a healthy diet. Healthy dietary patterns are those generally low in red meat, salt, and refined sugars, and high in oily fish, deep coloured fruit and vegetables, fibre, pulses, nuts, and whole grains. However, importance should not be given on single nutrient approaches. A more significant aspect is the wider dietary habits which involve consumption of several food groups, over long periods of time, rather than episodically. For instance, a Western type dietary pattern has a higher cardiovascular risk, compared to a consistent Mediterranean type diet (Najafi et al. 2020).

26.4 Cancer

It is beyond the scope of this chapter to discuss nutritional support for all cancers. However, it may be interesting to give a glimpse into the role of certain nutrients which, alone or in combination, could be used to improve cancer-related symptoms or risks. The following is a short list:

- Coriolus versicolor, an edible medicinal mushroom, consumed mainly in China. Two of its polysaccharides, namely CVPn and CVPa were shown to induce nitric oxide production, phagocytosis and reduction of Tumour Necrosis Factor (TNF) (Zhang et al. 2020). In other words, coriolus may exhibit increased immunomodulation and thus be useful in inhibiting the growth of cancerous cells.
- Resveratrol in association with curcumin. In a recent study, the combination of these two nutrients was found to enhance autophagy, modulate apoptosis and provide protection against cancer both in vitro and in vivo (Patra et al. 2020). Resveratrol is abundant in red wine, blueberries and dark chocolate, while curcumin is found turmeric. Both are also available in oral supplement form.
- L-carnosine (β-alanine, l-histidine). Found in red meat and game meat, carnosine is a pluripotent agent with a host of effects. Apart from acting as an antioxidant and

anti-glycator, it is a heavy metal chelator, and apoptosis modulator (Chmielewska et al. 2020). It has been used against several degenerative conditions, such as cataract, diabetes, cancer, neurodegeneration, and even schizophrenia (Banerjee and Poddar 2020). Carnosine will be mentioned again below.

- Chrysin (5,7-dihydroxyflavone) is found in honey, propolis, and passion flower. It exhibits antiproliferative activities and it can be used in association with conventional chemotherapy with cisplatin (Sherif et al. 2020). Its antineoplastic effect has been studied with regards to cancers of the lung, breast, colon, cervix, stomach, melanoma, and liver (Ganai et al. 2020), so it remains a promising agent.

The concept of calorie restriction mentioned above, can also be useful in the general case of cancer. Through a restrictive dietary pattern, it may be possible to activate autophagy, and this may have positive outcomes during chemotherapy. An increased dependency of cancer cells on autophagy may be exploited through nutritional interventions, although research on humans is still unsatisfactory (Cozzo et al. 2020). Autophagy is a process whereby dysfunctional or unnecessary cellular components are eliminated by the cell, and this mechanism has gained increased attention by researchers with regards to ageing. In any case, calorie restriction and/or intermittent fasting are known to exert benefits on insulin, IGF, cortisol, sexual hormones, oxidation, inflammation, as well as on markers such as FOXO, AMPK and SIRT-1 (Longo and Fontana 2010).

It is clear from the above short discussion, that nutrition plays an important role here and that research is confirming the beneficial action of several nutrients. However, it is also important to mention that it is unlikely that any single nutrient will have a noticeable effect. Best results may be obtained through a combinational nutritional approach, in association with other lifestyle measures, tailored specifically to the individual.

26.5 Age-Related Macular Degeneration

The subject of nutrition features high in the list of prevention measures recommended for Age-Related Macular Degeneration (ARMD). It is worth remembering that ARMD, together with glaucoma, are neurodegenerative conditions and are the leading causes of blindness in older populations.

Research in ARMD over the past several decades has examined the action of nutrients (vitamins/minerals/factors) such as vitamins C and E, beta-carotene, zinc, lutein, zeaxanthin, copper and the polyunsaturated fatty acid docosahexaenoic acid (DHA) among others (Walchuk and Suh 2020). Some of the recommended nutrients may exhibit hormetic (Rattan and Demirovic 2009) benefits, being beneficial in low doses and detrimental in higher doses. The typical example is resveratrol which inhibits neovascularization, reduces reperfusion damage and improves vascular serum biomarkers (Richer et al. 2013). Resveratrol is available mostly in red wine (hormetic doses!) and as an oral supplement.

Exogenous supplementation with NAD (nicotinamide adenine dinucleotide) has been found to play an important role both in therapy and in prevention (Cimaglia et al. 2020). NAD is a factor which regulates retinal cell metabolism and homeostasis, and mechanisms involved in this respect are the induction of mitophagy and the regulation of oxidative stress (Wei et al. 2019).

Several other nutritional manipulations have been associated with a decreased risk of ARMD. For example, a decreased omega-6/omega-3 ratio protects against neovascular ARMD (Mance et al. 2011). It has been suggested that a omega-6/omega-3 ratio of 1 is the normal evolutionary ideal for health, whereas in Western diets this ratio is as high as 15 to 1 (Simopoulos 2006). This increased ratio is associated with several other chronic conditions, including cardiovascular diseases, cancer and chronic inflammation, as mentioned above. In this respect, increasing the intake of omega-3 fatty acids should be the aim of dietary interventions. Therefor a diet rich in cold-water fatty fish (herring, tuna, sardines, salmon, and mackerel), in seeds/nuts (walnuts, flaxseed, soya bean, canola) or in the form of oral supplements, has been recommended (National Institute of Health, Office of Dietary Supplements https://ods.od.nih.gov/factsheets/Omega3FattyAcids-Consumer/, retrieved 20 January 2021).

Certain alternative interventions may also be of some use. A retrospective single-group study using a treatment modality based on intravenous nutrition in association with microcurrent stimulation and light therapy was found useful (Kondrot 2015). The authors of this study found significant improvements in visual acuity contrast and visual fields.

There are foods that are best avoided in ARMD. Examples include processed foods that contain trans fats, palm oil, lard, vegetable shortening, and margarine. High-fat dairy foods, fatty beef, pork and lamb are also to be avoided.

26.6 Menopausal Symptoms

Nutritional support for menopausal problems has been the subject of a large number of studies, for many decades. Nutrients or supplements studied include black cohosh, flaxseed, calcium, red clover, vitamin D, and, of course, soya. The following is a short comment on some of these, concentrating on the latest published research at the time of writing.

- Black cohosh *(Actaea racemosa, Cimicifuga racemosa).* In a systematic study it was found that black cohosh extract was significantly better than placebo in the treatment of menopausal symptoms, with no significant adverse effects (Castelo-Branco et al. 2020).
- Flaxseed. A very interesting study explored the relationship between lignan-rich oilseeds such as flaxseed oil, and the gut microbiota. The study showed that such oilseeds interact with faecal microbiota in premenopausal women and, through modulation of enterolignans, act as a substitute for human oestrogen (Corona et al. 2020). This leads to a better clinical profile, reducing menopausal symptoms.

- Soya genistein (Thangavel et al. 2019). One of the best studied elements of soya is the group of isoflavones (phytoestrogens), and specifically genistein. This forms a large part of the isoflavone content of soya, perhaps as high as 60%. Genistein improves glucose metabolism, induces apoptosis in cancer, has antioxidant effects, and modulates postmenopausal symptoms such as hot flushes, anxiety and depression.

Polyphenols (isoflavones, genistein etc.) exhibit a hormetic, biphasic dose–response activity. In other words, they are beneficial in low dose and detrimental in higher doses, having only a defined window of positive result, beyond which they become detrimental (Leri et al. 2020).

Apart from nutrients used to alleviate symptoms of the menopause itself, it is also necessary to consider nutrients which are of benefit in conditions associated with the menopause, such as osteoporosis. Vitamin D status can affect both menopausal symptoms and osteoporosis, as mentioned below. Dietary macronutrients such as vitamin D consumption may have a positive effect in this respect. It is known that serum 25-hydroxyvitamin D concentration is correlated with menopausal status, and that oral consumption of vitamin D may be able to modify any adverse effects associated with the menopause (Chun et al. 2020). Sources of dietary vitamin D include fish such as salmon, sardines, herring and mackerel, red meat and liver, egg yolks and specially fortified foods, and of course, as oral dietary supplements. It is worth mentioning at this point that vitamin D deficiency is widespread, including (paradoxically) in countries where there are long periods of sunlight. Levels of 25(OH)D below 30 nmol/L are encountered in over 20% of the population in India, Tunisia, Pakistan, and Afghanistan. Specifically, in India, it is estimated that half a billion people may have low vitamin D levels (Cashman 2020).

26.7 Osteoporosis

The case of osteoporosis is an example of the complexity of ageing, in the sense that it is not just one disease related to degeneration, but its presence is associated with other conditions affecting the elderly, such as frailty, falls, mobility problems, pain etc. In addition, it is an example of how a multifactorial approach to treatment is necessary. It is not enough to employ only a dietary or a pharmacological approach, but several other interventions need to be used in association, e.g. physical exercise, hormonal manipulation, and appropriate lifestyle measures. This underlines the requirement to deal with ageing in a multidisciplinary fashion, where treatment of one condition may have secondary beneficial effects on another. In any case, nutrition does play a significant role here, as obesity and osteoporosis are interrelated, and as it is known that the Western diet with its saturated fat content does influence osteoporosis (Martyniak et al. 2020). In this respect, polyunsaturated fats in the diet are beneficial because these reduce bone loss and enhance osteogenesis (Bao et al. 2020). Certain

other nutrients do have a proven benefit, and these include minerals (calcium, phosphorus and magnesium), vitamin D, vitamin B12 (Kalimeri et al. 2020) protein rich foods, fibre, fruits and vegetables, and prebiotic foods (Ilesanmi-Oyelere and Kruger 2020).

Other studies have shown the benefit of tomato (green tomato extract) which improves bone formation through Bmp2-Smad 1/5/8-Runx2 signaling, and modulate the nuclear factor kappa-B (RANKL)/osteoprogeterin (OPG) pathway, which in turn improves bone resorption (Nirmala et al. 2020). It is an opportunity here to mention that BMPs (Bone Morphogenetic Proteins), are members of the TGF-β superfamily, which have strong osteogenic activity and stimulate mesenchymal osteoprogenitor cells to become mature osteoblasts. This shows that nutritional factors may indeed modulate bone metabolism, therefore a wise dietary choice should have a positive therapeutic result.

A relevant vitamin not usually considered by nutritionists in osteoporosis, is vitamin K. This vitamin plays a role in cardiovascular health and in bone development, as already mentioned above in the case of osteoarthritis. The National Academy of Science (Food and Nutrition Board), has determined that the dietary requirements of healthy people are around 100 ug/day, but the requirements in older people with chronic degenerative conditions could be different. There is an intricate relationship between vitamin K, gut microbiota and osteoporosis. Certain intestinal bacteria produce vitamin K and thus affect bone metabolism, bone composition and, ultimately, fracture risk. The most relevant bacteria in this respect are those of the genus Bacteroides (fracture risk increases as their concentration decreases), and those of the Rikenellaceae family (Ozaki et al. 2020). Therefore, it is important to maintain good intestinal flora through use of probiotics (BOX 1). This will not only have an effect on bowel health but can also affect bone and even neuronal health, as mentioned below in the case of dementia.

26.8 Alzheimer's Disease

Among other factors, inflammation, and one of its markers, Tumor Necrosis Factor alpha (TNFα), have been implicated in Alzheimer's Disease (AD). A high-fat diet increases expression of TNFα in the tissues but this does not necessarily translate into a worsening cognition score (Jackson et al. 2020). There are multiple factors and processes contributing to AD and it would be simplistic to claim that a suitable nutrition will inevitably lead to a reduced risk of the disease. Nevertheless, it is possible to discuss some dietary factors that could possibly be useful, both in prevention and in patients with established AD. For instance, resveratrol could be of benefit, particularly if combined with physical exercise. The mechanism here could be due to resveratrol's effects on apoptosis, neuroinflammation and reduction of Aβ oligomers (brain amyloid-beta) (Broderick et al. 2020).

Enhancing mitophagy will be mentioned below, in the case of Parkinson's disease. However, mitophagy is also implicated in other neurodegenerative diseases including

Alzheimer's Disease. During mitophagy there is elimination of age-damaged mitochondria. Nutrients such as resveratrol, curcumin, astaxanthin and spermidine (which are found in the Mediterranean and Okinawan diets), are increasingly being promoted as effective in enhancing mitophagy (Varghese et al. 2020).

The relationship between the gut microbiota and chronic neurodegenerative conditions is increasingly being recognized, and has been briefly mentioned above. Dysregulation of the function of gut microbiota, affects the gut-brain axis and has repercussions on neurological function (Zhu et al. 2020). Therefore, maintaining an effective balance and function of the gut microbiota, usually through nutritional manipulations, should result in a decreased risk of neurodegeneration, including Alzheimer's dementia (Kowalski and Mulak 2019) (BOX 1). For instance, ketogenic diets and intermittent fasting were found to have an effect on Alzheimer's disease, at least in a rat model (Park et al. 2020). In this study it was found that intermittent fasting and a diet high in starch may decrease the progress of dementia. It is, however, suggested that because there is a great variation in the gut microbiota between people, it is necessary to tailor-made each intervention to optimally suit each individual.

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BOX 1

Ways to improve gut microbiota include (Valdes et al. 2018):

* Probiotics (Bifidobacterium and Lactobacillus species)
* Dietary fibre
* Avoidance of antibiotics, pesticides, and food additives, such as emulsifiers
* Fermented foods such as kimchi (fermented cabbage), sauerkraut, kombucha (a fermented beverage of black tea and sugar), kefir (fermented milk product), miso (fermented soybean, barley or brown rice), tempeh (fermented soybean product), raw cheeses made from unpasteurized milk, and Greek yogurt.

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The potential of carnosine against chronic degeneration has already been mentioned above, but it is worth returning to this nutrient as it appears to have a confirmed anti-neurodegenerative action (Schön et al. 2019). Carnosine is available in red meat and also as an over-the-counter food supplement. It can cross the blood-brain barrier, reduces amyloid beta polymerization, and decreases aggregates of amyloid. In addition, carnosine protects brain vascular endothelial cells (RBE4) against toxicity induced by beta amyloid, and modulates brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) in some animal models (Schön et al. 2019). Overall, it optimizes energy metabolism, improves the function of mitochondria in neurons and acts as a suppressor of chronic neurodegeneration, making it an ideal nutritional supplement in age-related brain diseases (Banerjee and Poddar 2020).

Also, at this point it is worth mentioning that a patient suffering from dementia is more likely to be frail, weak, and sarcopenic, with other concomitant conditions. It is therefore important to consider all aspects of health in this type of patient and establish a nutritional program suited to the specific (not the general) needs of each such patient.

26.9 Parkinson's Disease

Conditions which can contribute to the pathology of Parkinson's disease (PD) may include dysbiosis due to dietary habits, and increased intestinal permeability (Lister 2020). It may thus be possible to alter the progression of the disease by suitable manipulation of these nutrition-related conditions. Principal factors in this respect could be the status of vitamin D and B complex, omega fatty acids, probiotics and coenzyme Q10.

An interesting approach in Parkinson's disease is to modulate mitophagy, in other words, the elimination of damaged mitochondria, through nutritional factors. We know that there is mitochondrial dysfunction in dopaminergic neurons in PD, therefore any measures which may result in improved mitophagy may lead to an improvement in clinical symptoms. Promotion of mitophagy can be achieved through boosting of Parkin, a ubiquitin ligase, by consuming a low protein, plant-based diet (McCarty and Lerner 2020). This could be one of the reasons why East Asian and sub-Saharan Africa diets (mostly vegan) have a decreased risk of PD compared to the high protein diets of Western countries.

A diet rich in spermidine may also enhance mitophagy (Yang et al. 2020). Spermidine can be found in the components of the Mediterranean diet such as mushrooms, legumes, and whole grains, as well as in soy and corn. The role of spermidine in protecting against neurodegeneration in general (not only PD but also Alzheimer's disease, and ageing degeneration) is important and is slowly but increasingly being elucidated.

Hydrogen sulfide (HS) is a signaling molecule with multiple actions, and it exhibits typical hormetic properties. It provides protection against oxidative damage and it is also a cytoprotector. It plays a positive role in neurogenesis (Sun et al. 2020). N-acetylcysteine and methionine are precursors of HS, and are available in oral supplements. However, HS acts in a hormetic manner, meaning that while low doses can be of benefit, higher doses may be detrimental (Calabrese et al. 2010).

In addition, in PD there is generation of cytotoxic factors (such as peroxynitrite) by microglia, which then cause dysfunction of dopaminergic neurons. It has been suggested that modulation of peroxynitrite through nutritional factors may translate into clinical benefit in PD (McCarty and Lerner 2020). Compounds which may play a role in this respect include spirulina, vitamin D, caffeine, probiotics, promotion of hydrogen sulfide (taurine, N-acetylcysteine) and generally low-protein diets which may also help in improving response to levodopa drug therapy (Guebila and Thiele 2016).

Certain plant alkaloids, such as palmatine, have exhibited inhibition activities against anti-acetylcholinesterase, and are thus being studied further with regards to their phytotherapeutic effects against Parkinson's disease (Chaves et al. 2020). Palmatine is found in extracts of the Coscinium fenestratum plant, for example. It has several other health-improving properties, and it exhibits a hormetic, dose–response activity – essentially acting as a hormetin (Long et al. 2019).

Studies of diet patterns show that 'healthy' diets (such as the Mediterranean diet) are associated with a reduced incidence of prodromal symptoms of Parkinson's disease (Mosberry et al. 2020). Specifically, it was shown that increased adherence to a Mediterranean diet is associated with a corresponding decrease in the risk of non-motor prodromal symptoms of Parkinson's disease in older people, such as depression, constipation, urinary dysfunction and daytime somnolence (Maraki et al. 2019).

26.10 Sarcopenia

A common condition which contributes to physical frailty and falls in later life is sarcopenia. It is a progressive condition where there is loss of skeletal muscle mass and reduction of physical strength. Sarcopenia has been associated with low-grade chronic inflammation, with abnormalities in protein metabolism in the muscle tissues, and mitochondrial dysfunction. Clinically, it has been associated with several detrimental effects common in ageing, such as falls, hospitalization, chronic disability, and institutionalization.

An interesting view is that dietary interventions may influence miRNAs in muscle (myomiRNAs) which regulate development and maintenance of muscle tissue (Barbiera et al. 2020). Dysregulation of myomiRNAs is found in ageing (Drummond et al. 2008), and it has been shown that nutritional factors may play a positive role here (Iannone et al. 2020). See BOX 2.

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BOX 2

Nutrient-dependent miRNA regulation may be achieved with:

* Essential amino acids (EAAs), which increase miRNA function (Drummond et al. 2009)
* Glucose and amino acids (e.g. Leucine) (Chen et al. 2013)
* Albumin (Soeters et al. 2019)

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There are several studies confirming that certain nutrients may impact positively on sarcopenic patients. For instance, daily consumption of yogurt fortified with vitamins D (1000 IU) and C (500 mg) together with beta-Hydroxy beta-Methyl Butyrate (3 g) for 12 weeks in a randomized, double-blind controlled manner, was found to improve muscle strength and anabolic functions in older patients with sarcopenia (Nasimi et al. 2020). The role of beta-Hydroxy beta-Methyl Butyrate (HMB) in building muscle mass in sarcopenia is intriguing. It is a metabolite of leucine which regulates muscular protein synthesis and has a host of other actions (Cruz-Jentoft 2018). For instance, it:

- Decreases muscle cell apoptosis
- Stabilizes cell membranes
- Inhibits the ubiquitin-proteasome pathway, thus reducing proteolysis

- Enhances proliferation and differentiation of stem cells in muscle
- May prevent muscle loss in bed-ridden patients who cannot exercise

Therefore, although more studies are needed in order to confirm solidly the effects of HMB, it is fair to suggest that its use can help older people with sarcopenia, by improving lean muscle mass, muscle strength and physical function (Oktaviana et al. 2019). This nutrient is usually taken by mouth in powder form.

Royal jelly is another nutrient which may be helpful in sarcopenia. It delays muscular functional decline during ageing and prevents muscle fiber atrophy (Shirakawa et al. 2020). Royal jelly, and other bee products such as propolis and bee pollen, are rich in antioxidants with strong action, including flavonoids and phenols, as well as being rich in several amino acids. These can modulate inflammatory response and decrease oxidative and glycation stress in muscular tissues, reduce catabolic activity, improve stem-cell function, improve AMPK metabolism, and enhance muscle protein synthesis (Ali and Kunugi 2020).

The activity of AMPK (5'-adenosine monophosphate-activated protein kinase) is one of the most interesting subjects in the field of ageing. AMPK controls muscle metabolism and modulates anabolic and catabolic events. It improves muscle mass and muscle tissue regeneration (Thomson 2018). It is known that obesity is associated with a reduced AMPK function, although chronic activation of AMPK, is also found in obesity and in impaired pancreatic function. We see once again that hormetic, dose-response principles come into play, when long-term, indiscriminate activation of AMPK is not necessarily beneficial and should be avoided (Lyons and Roche 2018).

26.11 Benign Prostatic Hyperplasia (BPH)

Peanut sprouts (germinated peanuts) containing high amounts of resveratrol are eaten in salads or in stir-fries usually in a vegetarian diet context. Extracts of the Yesan sprout variety were found to affect molecular markers of BPH, such as 5α-reductase, fibroblast growth factor, and the apoptotic markers Bcl-2, and Bax. In model rats, the extract also reduced the size, weight and thickness of prostate (Song et al. 2020).

Nutritional habits which may affect zinc in men over 50 years old, can also affect the risk of BPH. Zinc has consistently been shown to play an active role in BPH, although it is not a simple matter of increasing the daily dietary amounts of zinc and expecting to see clinical result. Zinc metabolism depends on factors that may promote or hinder zinc absorption. These factors can be endogenous and/or exogenous, such as drugs or a diet low in zinc (Sauer et al. 2020). Zinc exhibits a concentration-dependent effect on inflammation, oxidation and apoptosis, through modulation of TNF-α and IL-6 (Hacioglu et al. 2020). Foods rich in zinc include oysters, red meat and poultry, beans, nuts, and whole grains.

Although it is known than cranberry extracts may have an effect on urinary tract infections, little is known about its effect on BPH. In a model using male Sprague-Dawley rats treated with cranberry powder, it was found that the extract has a significant decreasing effect on prostate weight, dihydrotestosterone (DHT), and 5-alpha reductase (An et al. 2020).

An interesting nutrient and hormetin in the case of prostate, is ginger. Hormetins are natural or synthetic compounds which can produce hormesis (Rattan and Kyriazis 2019). Ginger (*Zingiber officinale Roscoe)* has numerous effects including antidiabetic, lipid-lowering and anti-inflammatory actions. Its activities include apoptosis modulation, improvement of autophagy, and cell regulation. In addition, ginger has oestrogen-modulating effects which means that it can be beneficial in prostate hyperplasia, as well as in other conditions where oestrogen is involved (osteoporosis, menopause and certain cancers) (Kiyama 2020).

26.12 Conclusion

It is important to advise the patient that there is no universal diet or a nutritional pattern that can protect against all age-related diseases. Each disease, while sharing certain common characteristics of ageing (for instance oxidation, inflammation, degeneration, and glycation), has to be seen separately and focused on the needs of each particular patient. The principles of personalised medicine should be applied in all aspects of nutritional interventions, both for prevention and for treatment. It is known that diets which are generally considered 'healthy' in some countries (e.g. Mediterranean diet) may not be suited to the cultural, social or biological makeup of other countries (Asia, for instance) (Moffat and Morell-Hart 2020). Therefore, a dietary pattern has to be tailored individually to each patient, and be considered with other lifestyle measures, specific to that patient. Nevertheless, there are certain pluripotent nutrients that can be recommended in most conditions. Examples include resveratrol, carnosine, omega-3 acids, and vitamins D, E and C.

Nutrition may help in the prevention and treatment of age-related degenerative conditions through modulation of oxidation, glycation, inflammation and cell metabolism. It is not, however, the only important factor in these conditions, neither it is an approach that can work on its own, separate from other lifestyle interventions. The interaction between nutrients and physical exercise, smoking and excess alcohol, as well as genetic factors, play an intricate role in achieving optimal health for the ageing patient. Research has clarified a great amount of basic biological mechanisms of how this can be achieved. The study of these mechanisms provides useful insights regarding the mechanisms of ageing, hormesis, and optimal clinical function in ageing.

Compliance with Ethical Standards

Conflict of Interest All authors declare they have no conflict of interest.

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