The Fact and Fiction of Nutritional Claims About Health and Longevity

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Abstract

For centuries, various feeding regimens have been proposed to live longer with a better health. However, in many cases, they have not been proven to have any positive effect, and they can even have negative ones. This chapter reviews the claims of various regimens (e.g. detox diets, fasting). It is doubtful that they could increase human lifespan and improve health, provided one adopts a balanced regime with no excessive intake and avoids junk food.

1. Introduction

For centuries, various regimes have been proposed to live longer and provide a better health (see the chapter 25 in this book: Stambler 2020a; Haber 2004; Stambler 2020b). Modulating food intake appears as an obvious strategy to improve health because everybody has observed that gluttony or famine bring with them a bad health. Going a step farther, it could be expected that modulating both the quantity and quality of food has beneficial or deleterious effects on healthspan and, ultimately, on lifespan.

One of the first modern claims that a specific food could have such effects was that of the 1908 Nobel laureate Elie Metchnikoff, who wrote (translated from French) that "the introduction of microbes cultivated from sour milk can bring about a considerable change in the intestinal flora in a direction favourable to the preservation of health … (and) making old age more physiological than it is at present and probably also of prolonging human lifespan" (Metchnikoff 1903). This was the beginning of the yoghurt industry (Fisberg and Machado 2015) and the good news is that eating yoghurt does not provoke any harm. This is however not the case with all regimens claiming to increase lifespan. One of the issues with such regimens is that fear of aging can lead many people to support them despite any counter-argument. Because this behaviour is not only that of adepts but can also be that of scientists, the net result is that some people are even more convinced that they adopt the best way to live long if they eat a specific food, ingest antioxidants, or fast. Partly connected to this issue is that of fashion. From time to time, a new long-life recipe shoots to the fame and many people are immediately convinced of it, before giving up when a new recipe is proposed on the TV, magazines or social networks. This is an issue because, in some cases, these recipes are dangerous and it has been warned that "some dietary supplements have been associated with potentially serious health consequences for senior citizens" (United States General Accounting Office 2001).

Therefore, fear of ageing, fashion, or over-enthusiasm of the lay public and scientists are obstacles to know the merits and pitfalls of regimens and/or individual nutritional components

claiming to improve life at old age, or even to live longer, and this should be taken into account when reviewing the effects of these regimens. The purpose of this chapter is to separate the fact and fiction of nutritional claims about health and longevity.

2. Vitamins and other micro-nutrients

Vitamins are often considered by the lay public to be "good" because of their name, vitamin meaning life and amine, and of their association with fruits and vegetables. Most of people know that a lack of vitamins can provoke severe health issues and some think that the higher the dose, the best is the effect on health. While the first part of this sentence is correct, the second one is not. However, relying on this wrong rationale, many people, including some scientists, believe that one should supplement food with vitamins, even if it already contains a large part of fruits and vegetables. The first issue is that high doses of some vitamins can be toxic, as it is the case with vitamin E (Miller et al. 2005; Bjelakovic et al. 2007). The second issue, less tragic, is that high doses can be not assimilated and are excreted, like vitamin C in urine. Nevertheless, the double Nobel laureate Linus Pauling promoted high doses of vitamin C because "vitamin C will have great value in controlling the problems associated with advancing age" (Pauling 1983) and also "improve the general health of nearly every cancer patient (and) increase survival time somewhat" (Pauling and Moertel 1986). Regarding this claim of Pauling on cancer, Moertel, in the same two-handed article, severely wrote: "Whether one is dealing with treatment of the common cold or of cancer, and whether one is dealing with a benign vitamin or a highly toxic chemotherapeutic drug, it would seem to best serve the interest of the patient if public advocacy of a proposed treatment is withheld until that treatment has been proved effective by definitive studies of sound scientific design".

In any case, the opinion of a Nobel laureate can lead to major consumption changes and the main result is that, nowadays, the internet is replete with sites promoting vitamin C. The Nobel laureate Elie Metchnikoff provoked the birth of a new industry, that of yoghurt, and the Nobel laureate Linus Pauling made that many people take 1 g or more of vitamin C daily and produce an expensive urine, for the best of pharmaceutical industry. The difference is that yoghurt is a food, and thus useful, and that taking 1 g of vitamin C daily is useless, particularly if people eat fruits.

Beside vitamins, other micro-nutrients, such as mineral ones, are advertised and sold as recipes to live longer. For instance, selenium (Se), which is involved in antioxidant enzymes such as glutathione peroxidase, is sold on the internet for "optimized health and longevity support". However, while selenium deficiency can be an issue, for instance in Sweden (Alehagen et al. 2016), and "may suggest the value of modest Se supplementation in order to improve the health of the Swedish population", it is not the case in the USA, a result which pleas against supplementation

because the window for therapeutic effects is narrow and toxic effects are soon observed (references in Bleys et al. 2007). Yet, dozens of selenium supplements are for sale in the USA.

3. Antioxidants

The free radical theory of ageing (Harman 1956) posits that ageing "seems to be a more or less direct function of the metabolic rate", as it was postulated by Pearl (1928) in his rate of living theory, and that, because "the concentration of free radicals increased with increasing metabolic activity", antioxidants could "slow down the aging process and thereby put off the appearance of the diseases associated with it". This theory gained early a very large popularity because it was easy to understand: a higher metabolism means more radicals, more attacks, and thus a shorter life. In fact, Harman (1956) provided the biochemical mechanism of the postulated negative effect of metabolism on lifespan. However, it seems clear for many years, among species (e.g. Austad and Fischer 1991) or in the same species (e.g. Lints 1989), that a higher metabolism is not linked to a lower lifespan. Furthermore, the free radicals theory of ageing does not seem to explain lifespan. For instance, among 13 primate species, Csiszar et al. (2012) concluded that "increased longevity in this sample of primates is not causally associated with low cellular reactive oxygen species generation". Within species, Le Bourg's reviews (2001, 2003, 2005) concluded that it is doubtful that antioxidants could be of help to increase lifespan in animal models or in human beings.

Finally, Speakman and Selman (2011) wrote that there are "fundamental questions over whether the free-radical damage theory remains useful for understanding the ageing process". These authors emphasised that "it has been recently suggested that perhaps the lifespan effect is too harsh a criterion by which the theory should be evaluated", but one can bet that if clear effects of antioxidants had been observed on lifespan, it would not be considered "too harsh a criterion". The authors argued that focusing on health is more sound because oxidative stress is linked with various diseases. For instance, cataract is linked with a depletion of glutathione but, for the time being, "antioxidant supplementation has been shown to be ineffective in preventing or delaying cataract" (Lim et al. 2020). Beyond cataract, Luo et al. (2020) put the last nail in the coffin, concluding that "while observational studies mainly found detrimental effects of high oxidative stress levels on disease status, randomized clinical trials examining the effect of antioxidant supplementation on disease status generally showed null effects".

In such conditions, why taking antioxidants to delay ageing and increase lifespan? There is simply no reason to do that because, after decades of research, supplementing food with antioxidants has not been shown to have any effect. Yet, it remains that there is a plethora of antioxidants on the internet, for the best of companies selling them.

4. Other dietary supplements

Companies have an innumerable imagination when they intend to sell dietary supplements, as it can be easily seen on the internet when typing “dietary supplements aging” and selecting “shopping”. In addition to vitamins and antioxidants, many other supplements are for sale, and it would be a waste of time to enumerate all of them. Just focus on a famous one, because advertised, again, by a Nobel laureate.

Fermented papaya was promoted by the 2008 Nobel laureate Luc Montagnier as having anti-ageing effects and boosting antioxidant defences. It was particularly proposed in 2002 to the pope John Paul-2 as a remedy against the Parkinson’s disease. In 2004, the French food safety agency concluded that there was not any evidence for an anti-ageing effect and that (translated from French) “the use of recommendations by scientific personalities, which is decried in the context of the promotion of pharmaceutical products, is not acceptable for foodstuffs either” (AFSSA 2004). Since then, a few articles have been published, not always in well-known journals, and it seems that fermented papaya has not shown a significant amount of positive effects on the ageing process, which could induce its use as a classical drug.

This is probably the final word about dietary supplements: if some scientists think that the supplement X can be of use to improve or delay ageing or increase lifespan, it is incumbent upon them to work with pharmaceutical companies to test their expected new anti-ageing drug according to the usual rules. If X eventually appears to be of some use, more than a placebo, it will be incorporated in the list of authorised and prescribed drugs. If it is not the case, X will be one of the numerous disappointing hopes, a common fate when testing new drugs. By contrast, promoting X in the mass-media without sticking to this process is an abuse of the public credibility.

5. Specific regimens (Mediterranean, unbalanced, and Okinawa diets)

Beyond the various supplements, several diets have been proposed to live long with a good health. The most famous one is probably the Mediterranean diet with many fruits and vegetables rather than excessive meat and fats. This diet seems to favour a better healthspan (e.g. Féart et al. 2010) and reduce all-cause mortality (e.g. Eleftheriou et al. 2018). It is not clear whether individual components of the Mediterranean diet explain its positive effects, as each component may have a slight positive effect, if any (Eleftheriou et al. 2018). However, it seems clear that people eating fruits and vegetables are less prone to eat junk food and thus eating more fruits is also eating less junk food. This way, adopting widely the Mediterranean diet could reduce the global threat of

obesity and cardio-vascular diseases (GBD 2015). It is not so surprising that this diet has positive effects on health or, rather, not-deleterious effects. Indeed, eating fruits and vegetables, proteins coming from fish and other animals, is not really different from the diet of the human kind for millennia. It is highly different from the consumption of excessive sugar, soft drinks, junk food and other modern foodstuffs not conceived to provide appropriate calories and a balanced regimen with lipids, proteins and carbohydrates, but to be massively sold with the lowest possible price and the highest profit. This Mediterranean diet thus appears to be a traditional feeding regimen but it should not be confused with the so-called paleolithic diet, which promotes 34% of calories coming from proteins (Eaton and Konner 1985). This paleolithic diet does not seem to be linked with beneficial effects on health (Dinu et al. 2020), which is maybe not surprising because a 35% level of proteins is dangerous as it exceeds the capacity of the liver to convert nitrogen in urea (Bilsborough and Mann 2006).

Beside the non-balanced paleolithic diet, other regimens have been proposed with either a low of high level of proteins, carbohydrates or lipids. Using a non-balanced regimen appears to be an error from the beginning, as it artificially alters the spontaneous feeding choice, because subjects forced to ingest an unbalanced diet could tend to reestablish their nutritional target as soon as possible. For instance, Simpson et al. (2003) showed that people fed for two days with a diet containing much more than the usual 15% of calories coming from proteins decrease their food intake by nearly 50%, with the result that the total consumption of proteins is hardly modified. Conversely, subjects forced to eat less proteins for two days increase their food intake by nearly 35%, the total consumption of proteins being also hardly modified. Thus, subjects eat less in the first case and more in the second one, because they strictly regulate the intake of proteins rather than the number of calories. Could it be that one of the causes of the epidemic of obesity in the USA is the decrease of the protein content, from 17% of calories in 1971-1975 in the US diet to a nadir of 15.1% in 2001-2002 (Ford and Dietz 2013), and the necessity of an increased food intake to eat enough proteins?

Similarly, it has been claimed that the Okinawa diet could improve health and increase lifespan (Willcox et al. 2006). The feeding regimen observed after World War 2 and up to the 1960s was depleted in proteins (9% of calories), which makes that, combined with a low number of calories (1785 kcal/day), Okinawans ate ca 57% of the proteins eaten by other Japanese people (Le Bourg 2012). This covers respectively, only 55, 70 and 84% of the daily protein needs of pregnant women, adult men and women (Committee on dietary references intakes 2005). In 1950, ca 20% of Okinawans had therefore nutritional deficiency symptoms, such as a delayed menarche for 10% of women and a deficient lactation for 18% of them (Willcox et al. 2007). Regarding lifespan,

Okinawans outlived other Japanese people when the infant mortality was twice higher in mainland Japan (e.g. 90‰ in 1940) than in Okinawa (45‰), which obviously decreased mean lifespan on mainland, but this higher lifespan in Okinawa does not longer exist today (Le Bourg 2012). Today, the malnutrition linked to World War 2 is over, and there is no doubt that the traditional Okinawan diet, with vegetables, sweet potatoes, and soy (Willcox et al. 2006), is of a better quality than the modern occidental food with soft drinks, junk food and so on. Yet, it seems there are no results showing that the Okinawan diet can increase lifespan (Le Bourg 2012), as claimed by some authors (e.g. Willcox et al. 2006).

6. Dietary restriction

Restricting the food intake is called dietary restriction (DR), but also calorie restriction or food restriction. Whatever the term, it means a decrease of food intake without malnutrition. It has been claimed that DR "will extend the life of all species in the Animalia kingdom, including the human species" (Masoro 2006) and that "it would be surprising if appropriately applied, chronic DR would not significantly increase the average lifespan of people" (Weindruch 2006). These very optimistic claims are however maybe not warranted because, even if it is often claimed that DR increases lifespan in many species, if not all, it is not the case (Le Bourg 2010), and, among mice, the results are dependent on the genetic background (Liao et al. 2010). In non-human primates, it has been reported that DR increased lifespan in the mouse lemur *Microcebus murinus* (Pifferi et al. 2018) and one of the two studies in the macaque *Macaca mulatta* also reported a higher lifespan in food-restricted animals (Colman et al. 2014; Mattison et al. 2012). However, these results are better explained by a low lifespan in the control group because of a bad diet and/or overfeeding (Le Bourg 2018).

Regarding humans, results on people self-practicing DR or in controlled studies, such as CALERIE (e.g. Ravussin et al. 2015) show that DR can decrease weight, body-mass index, body fat, cholesterol level, triglycerides, blood pressure, fasting glucose and insulin level (Fontana et al. 2004). All these indices are predictive of a better cardio-vascular health. However, body temperature (–0.2°C, Heilbronn et al. 2006), lean mass (–5%, Racette et al. 2006), muscular strength (–7%, Weiss et al. 2007), mineral bone density, particularly on hip (Villareal et al. 2006), can also decrease. A more recent study concluded that while DR decreased absolute muscle strength, it increased the strength when expressed relative to body weight (Racette et al. 2017), which could suggest that DR had no real negative effect. However, one can oppose that a DR subject would have more difficulty to carry a 20 kg concrete block than before beginning DR, and

that having a higher strength when expressed on the body weight would be of no help to carry the load.

It is not to say that DR protocols are useless as they could provide clues to fight obesity but it is not sure that DR could improve health of people of a normal weight, with an appropriate diet and making some exercise, thus, to people already applying well-known recipes to avoid a premature death. Furthermore, "people with a low body-mass index (BMI, say below 21kg/m^2) should also be cautioned against practicing CR, as they could soon become underweight, which is a risk factor for various health concerns" (Le Bourg and Redman 2018). It could even be said that DR could be risky for lean people, as adverse events linked to DR (infections, gastrointestinal disorders, and so on) are more probable in subjects with a normal body mass index (BMI: 22–25 kg/m^2) than in overweight ones (BMI: 25–28 kg/m^2) (Romashkan et al. 2016; Le Bourg 2018). Le Bourg and Redman (2018) have warned that DR "with the aim of delaying aging and increasing longevity is not an approved treatment for self-administration", and particularly that "the risk for elderly people is often not to eating too much, but eating too little", because there is a severe risk of undernutrition in elderly people (Kagansky et al. 2005).

However, other authors do not hesitate to write that people should consume starch and fat blockers in addition to a moderate DR (Kurzweill and Grossman 2010), despite the fact that starch and fat blockers are drugs with side-effects. They are prescribed against diabetes and obesity and certainly not in the absence of any disease, even if the internet is replete with advertisements for these products. Similarly, other authors claim that DR could be useful to people, like Most et al. (2017) who write that a forced 20% DR without malnutrition during World War 2 in Norway made that mortality from cardio-vascular diseases dropped by 30%. Because the cited study of Strøm and Jensen (1951) reports a very "close correlation" with the up to 40% decrease of fat intake, it could be concluded that DR decreased mortality but tobacco consumption also decreased by ca 50% during the war (Lund et al. 2009). It is not a risky hypothesis to state that this decreased consumption of tobacco had probably a huge effect on cardio-vascular mortality.

DR is a procedure used in laboratory and clinical studies to better understand, particularly, how to decrease the toll of obesity or cardio-vascular diseases. However, it is a risky business if not done in a controlled study in a laboratory under strict supervision of physicians. Thus, people involved in, for instance, the CALERIE study are not at risk, but those who decide to restrict their food intake on their own are at risk, particularly if they are rather old. It is maybe not surprising that DR is so fashionable in the USA, because obesity is an important problem for a large part of the US population. One may argue that people wishing to live long and not to become obese should first adopt safe behaviours: discarding junk food and snacking, eating more moderately than the current

US food intake, making exercise. It is often a hard challenge to modify a behaviour, particularly when the social environment does not encourage to do it, but it is the price to pay to enjoy a better healthspan.

7. Detox diets

For many decades, not to say centuries or millennia, some people have claimed that the organism could be auto-intoxicated and that it was necessary to clean the intestine, as narrated by Frexinos (1997). This way, various recipes have been proposed to clean the body and, more precisely, the intestine with purges (e.g. Guelpa 1910). Today, colon cleansing, or colon hydrotherapy, is still in favour but the so-called detox diet, which is in essence very similar to these old ideas, is more fashionable. While a very few people adopt colon cleansing to detoxify their body, there are numerous proposals of detox programs combining fasting, specific foods to clean the body, and physical exercise. However, "commercial detox diets rarely identify the specific toxins they aim to remove or the mechanisms by which they eliminate them" (Klein and Kiat 2015). These authors, reviewing the very few results on detox diets, concluded that "considering the financial costs to consumers, unsubstantiated claims and potential health risks of detox products, they should be discouraged by health professionals" and, very wisely, that "there is no doubt that sustained healthy habits are of greater long-term value than the quick fixes offered by commercial detox diets". There is not a single word to add.

8. Fasting

DR is not an easy way of life. Indeed, only a very few people are ready to restrict their food intake for years or decades in the hope to live longer. In a way, it is accepting a boring life and hoping it will last for longer than for other people, which is not very enjoyable. It would be much better if a short DR, or repeated short bouts of DR (intermittent fasting), could be used with the same results.

Fasting may have positive effects on health and survival to some threats. In *D. melanogaster* flies, fasting increases survival to anoxia, a model of ischemia-reperfusion in flies (Vigne at al. 2009), or to cold (Le Bourg 2013). A 3-days fast with water increases survival in mice subjected to renal ischemia-reperfusion, similarly to a 4-weeks DR (Mitchell et al. 2010). One week after reperfusion the 10 fasted and 10 DR mice were alive but only 4 out of 10 of control ones. In addition, fasting with chemotherapy helps mice to survive an artificial cancer more than chemotherapy alone (Lee et al. 2012). In women with breast cancer, a randomised clinical trial (de

Groot et al. 2020) with 131 patients suggested that fasting before chemotherapy could reduce the tumour more than chemotherapy alone in a per-protocol analysis (comparing patients that really complied with the protocol), the results being less clear in intention to treat (groups are compared even if some subjects did not respect the protocol, as in real life). Fasting is thus studied by scientists and, for instance, some authors wonder whether a preoperative fasting lasting more than the usual night could improve surgical outcomes (Longchamp et al. 2017).

Therefore, fasting seems promising in therapy and some authors highly promote it in books or media, as for instance Valter Longo (2018). Intermittent fasting is also fashionable and, at a first sight, it could appear as a nice idea to preserve health and, again, there are many sites promoting fasting cures on internet (e.g. in the US, https://thefastingmethod.com/, in France https://www.ffjr.com/) or in books. One of the issues with intermittent fasting is that some authors are over-enthusiast to the point they write problematic sentences. For instance, de Cabo and Mattson (2020) write that "on the island of Okinawa, the traditional population typically maintains a regimen of intermittent fasting and has low rates of obesity and diabetes mellitus, as well as extreme longevity". However, such "extreme longevity" does not exist (see above) and the Okinawa diet is not intermittent fasting: there is no fast for one or two days from time to time, but an avoidance of eating at satiety. In addition, writing that "clinical studies have focused mainly on overweight young and middle-age adults, and we cannot generalize to other age groups the benefits and safety of intermittent fasting", is hazardous, as the main issue in elderly people is under-nutrition: it would be risky for elderly people to fast more than they already and non-intentionally do.

People practicing intermittent fasting often say they feel better, with more energy. This is true and can be easily explained. When a subject or an animal is fasting, the nutritional needs are no longer satisfied, and the organism sounds the alarm to implement various means to restore the previous physiological state. Thus, more energy is diverted to seek food, at the expense of body reserves, cognition is in alert to locate food, and so on. As said by Longo and Mattson (2014), "hunger is an adaptive response to food deprivation that involves sensory, cognitive and neuroendocrine changes that motivate and enable food-seeking behaviors". The net result is that animals or subjects are better at walk and people have the feeling they have a better mood and cognition. A part of this process has been observed in *D. melanogaster* flies by Connolly (1966). Flies deprived of food put in a novel environment maintain a high activity level for at least 7 hours, while ad libitum-fed flies show a regular time-linked decrease.

This is what happens… at the beginning. After that, if fasting lasts for too long, the available energy is decreasing and subjects can become sluggish, physically and mentally. In other words, not

too old people with a good health are not at risk if they decide to fast for one day from time to time. Concluding that because they feel better, more awake, and even smarter, intermittent fasting will improve healthspan and even increase lifespan is an illusion linked to the physiological state occurring during a short fasting. It has been shown that regular fasting during the whole life (4 days every 2 weeks) could increase lifespan in mice (Sogawa and Cubo 2000), but it also paradoxically increased their weight. This is probably not the result hoped by people prone to fast, but it is also commonly observed in people under a restricted regimen. They lose weight, before often to regain more, probably because the organism is preparing to a next fast by making more reserves than before the fast: once bitten, twice shy!

9. Conclusions

For centuries, if not millennia, people have hoped to enjoy a better health by modifying their diet. It is a sound idea and there is no debate on the necessity to favour a regimen covering nutritional needs, but not more. However, it is not sensible to think that miraculous regimens do exist: if it were the case, humans would have discovered them since time immemorial. In fact, humans have discovered the miraculous regimen for a long life: a balanced regimen providing proteins, lipids and carbohydrates, as well as essential nutriments such as vitamins. Thus, a wise strategy is to discard modern junk food known to favour cardio-vascular diseases and, eventually, a shorter lifespan. Yet, it is also wise to resist ads promoting risky regimens with no proteins, or only proteins, dietary supplements daily, detox diets, and all new avatars of the modern quacks wearing a white blouse on a computer screen.

The global obesity epidemic is a real issue and the Covid-19 pandemic has shown that, among the younger patients, those transferred in intensive care units were often obese (e.g. Hajifathalian et al. 2020) and also that obesity increased the fatality risk (de Larochelambert et al. 2020). It is maybe a sufficient reason to adopt an appropriate food regimen and to discard other ones.

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