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Editorial

Fruit and Vegetables and Cardiovascular Health

Recent results from the Women's Health Initiative indicate that a diet low in fat but high in fruit, vegetables and grains does not significantly reduce the risk of cardiovascular disease in postmenopausal women. These results were unexpected and almost shocking, seemingly reversing the evidence from previous studies that was thought be solid. Despite these findings, other randomized studies strongly suggest that dietary changes can have beneficial effects on several cardiovascular risk factors, among them blood pressure, lipid levels, homocysteine levels, oxidative stress, inflammation, and endothelial function. Also, a large number of prospective observational studies support that particularly high fruit and vegetable consumption is beneficial, reducing the risk of cardiovascular events. A greater dietary change than the one achieved in the Women's Health Initiative is probably necessary to have an impact. That higher fruit and vegetable consumption as part of a healthy diet reduces blood pressure has been convincingly shown, but there is also evidence that it is related to lower increases in blood pressure over the life course. Potential nutrients involved include fiber, potassium, magnesium, vitamins, and antioxidants. For potassium, the evidence from supplementation trials strongly suggests that it in part explains the beneficial effects of fruit and vegetables on blood pressure. Although folate has a well-proven effect on plasma homocysteine concentrations and antioxidant vitamins have been demonstrated in experimental studies to reduce oxidative stress, clinical trials on folate or vitamin E supplementation among patients with CHD have been largely disappointing. The lack of primary prevention studies and the partly non equivalence of supplements to the natural form limit the usefulness of these studies. In addition, the abundance of a variety of antioxidants and other beneficial nutrients, like potassium and fiber, in fruits and vegetables highlight that emphasizing higher fruit and vegetable consumption instead of supplements will reduce the burden of cardiovascular diseases in Europe. The evidence, despite the null results from the Women's Health Initiative, is overwhelmingly supportive here.

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Potassium and its role in reducing arterial blood pressure

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High blood pressure is a major public health issue. There is an urgent need for population-wide strategies based on efficient diet and lifestyle approaches for preventing and treating high blood pressure in replacement or as a complement to pharmacological treatments. Increasing potassium intake by consuming a diet rich in fruits and vegetables is one of these approaches that should be promoted in developed and developing countries.

High blood pressure is a major cause of morbidity and mortality

High blood pressure (systolic pressure above 115 mm Hg and/or diastolic pressure above 75 mm Hg) is one of the leading causes of disability adjusted life years (sum of the years of life lost due to premature mortality and the years lost due to disability) in developed and developing countries[1]. There is an exponential relationship between blood pressure levels and the risk of ischemic heart disease and stroke. Despite progress in prevention, detection, treatment and control of high blood pressure, much remains to be done to solve this public health issue. Until now, the medical approach has only been focused on the few individuals at high cardiovascular risk (systolic pressure above 140 mm Hg and/or diastolic pressure above 90 mm Hg), ignoring the large number of individuals at low risk (systolic pressure between 120 and 140 mm Hg and/or diastolic pressure between 75 and 90 mm Hg) although over half of the cardiovascular events related to high blood pressure occurs in low-risk individuals[2]. Even in high-risk individuals, the overall control of high blood pressure remains low (only 10 % in 35-64 year old individuals) due to the insufficiencies of detection and treatment[3].

Diet and lifestyle recommendations for the prevention and treatment of high blood pressure

Current recommendations involve a population-wide strategy based on several approaches with proven efficacy for preventing blood pressure increase in low-risk individuals and for decreasing blood pressure in high-risk individuals: engage in moderate physical activity, maintain normal body weight, limit alcohol consumption, reduce sodium intake and maintain adequate intake of potassium by consuming a diet rich in fruits and vegetables[4]. These approaches have additive effects on blood pressure and should be used in combination even though they are not always easy to implement for economical, political and social reasons.

Blood pressure and fruit and vegetable intake

In the 1980s, vegetarians were found to have lower blood pressure than the general population and vegetarian diets were shown to decrease blood pressure[5]. More recently, transversal and prospective studies have reported an inverse relationship between blood pressure and fruit and vegetable intake[6]. Clinical trials have confirmed the antihypertensive effect of a high fruit and vegetable intake per se or in the context of combined interventions[7]. In parallel, several prospective studies have reported an inverse association between fruit and vegetable intake and cardiovascular risk[8].

Potassium probably explains in part the antihypertensive effect of fruits and vegetables

The hypothesis that fruits and vegetables lower blood pressure due to their high antioxidant content is supported by observational data but is not confirmed by intervention studies[9]. In contrast, there is strong evidence that the high potassium content of fruits and vegetables may explain, at least in part, their antihypertensive effect. Indeed, epidemiological studies show the existence of an inverse relationship between blood pressure and potassium intake: for example in the 52 populations of the 'Intersalt study', the increase of systolic pressure between 25 and 55 years of age differs by 14 mm Hg when daily potassium intake differs by 1.9 g[10]. Clinical trials demonstrate that increasing daily potassium intake by 2 g during a few weeks lowers systolic and diastolic pressures by 4.4 and 2.5 mm Hg[11]. Increasing potassium intake also reduces the need of antihypertensive medication for controlling high blood pressure[12]. Most of the trials have used potassium chloride for supplementing the diet while potassium in fruits and vegetables is mostly present as organic salts (citrate, malate). If the antihypertensive effect seems to be equivalent[13], organic salts have additional beneficial effects on calcium urinary excretion, kidney stones and bone loss due to their potential to generate bicarbonate in the organism[14].

Mechanisms of the antihypertensive effect of potassium

There is substantial evidence that potassium lowers blood pressure by causing urinary sodium and water loss in the same way as diuretics[15]. This explains why the antihypertensive effect of potassium is strongly dependent on sodium intake, the effect becoming larger when sodium intake increases. Potassium has also a direct effect on the arterial wall that may intervene in blood pressure regulation and in the development of vascular disease[16].

Practical advice

From an evolutionary viewpoint, the human body has evolved in a potassium-rich and sodium-poor environment and is therefore adapted for secreting large amounts of potassium and retaining as much as possible sodium[17]. Based on investigations in hunter-gatherer populations and in traditional rural societies, physiological daily potassium intake is probably over 10 g. In comparison, the average potassium intake in France, United-Kingdom, United-States and Italy is currently close to 3 g with a large inter-individual dispersion from less than 1 g up to 10 g per day. Thus, the vast majority of individuals in industrialized countries ingest less or much less potassium than needed[18]. The general advice is therefore to increase the consumption of food items like fruits and vegetables which contribute the most to potassium intake.

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Folates and/or antioxidants and their role in protecting against cardiovascular iseases

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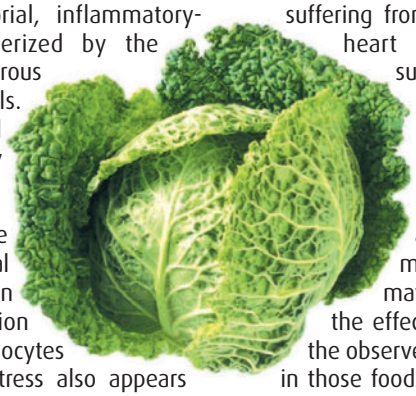
Cardiovascular diseases (CVD) account for almost 35% of all deaths in France and nearly 50% in industrialized countries. Though CVD mortality has been decreasing over the past 50 years, the global burden of the CVD is still very high with an increase of the prevalence of atherosclerosis, a multifactorial, inflammatory-degenerative disease of arteries, characterized by the accumulation of lipids (cholesterol) and fibrous elements in the wall of large vessels. Atherosclerosis is the pathophysiological substrate of the majority of acute coronary syndromes and ischemic cerebral strokes.



Oxidative damage of the arterial wall by free radicals and the direct stimulation of endothelial cells by the acute-phase C-Reactive protein promote the expression of cellular adhesion molecules which facilitate the adhesion of monocytes and T cells to the arterial wall. Oxidative stress also appears responsible for the oxidation of LDL incorporated into the plaque. Possible causes of endothelial dysfunction also include high plasma homocysteinemia.

Reactive oxygen species (ROS) are thus thought to be implicated in the pathogenesis of atherosclerosis since they are capable of damaging biological macromolecules such as lipids (e.g. fatty acids in LDL particles). The organism maintains defence against ROS, including enzymes and low molecular-weight antioxidants. An important source of antioxidants is diet which contains numerous compounds exhibiting antioxidant activity. Natural antioxidants are a group of substances able to counteract the oxidative damage.

Many moieties seem to prevent or interrupt the peroxidative chain in the human body: tocopherol and its isomers, carotenoïds, ascorbic acid, glutathione and other sulphydryl-containing molecules, flavonoïds...

Consumption of fruit and vegetables, olive oil, cocoa, red wine, and tea is inversely correlated with heart disease rates. These foods are particularly rich in natural antioxidant nutrients, including ascorbate, the tocopherols, carotenoïds and flavonoïds, naturally occurring substances which provide texture, colour and taste to plant foods.

Folates (vitamin B9) are also involved in cardiovascular prevention, through its well-proven effect on plasma homocysteine concentration, since a high nutritional intake may decrease hyper homocysteinemia which favours endothelial dysfunction and thrombosis. Folates are mainly found in dark green vegetables, legumes, some fruit, and in some animal foods including certain fermented cheeses and liver.

Many data are currently available on the oxidation and inflammation hypothesis of atherosclerosis and on the role of diet. Numerous epidemiological, clinical and experimental studies confirm that oxidized lipids accumulate in atherosclerosis lesions at all stages and that dietary antioxidants may reduce atherosclerosis progression. Moreover, several studies have shown that subjects suffering from a symptomatic atherosclerosis or from coronary heart disease (CHD) had higher levels of oxidized substances or markers of oxidized LDL, and/or lower levels of antioxidants compared to healthy controls.

Many epidemiological and clinical studies have shown that intake of antioxidant-rich foods, plant foods and particularly fruits and vegetables, are associated with lower occurrence of CVD. Similarly many studies have shown that high intake of folic acid may prevent strokes. But it is very difficult to separate the effect of one antioxidant from another and to attribute the observed benefit to a specific food since they are associated in those foods and in the global diet. Interventional randomized controlled trials have thus been conducted to prove the responsiveness of one or more antioxidants in reducing the progression of atherosclerosis or the occurrence of CHD. In many cases these studies have failed to demonstrate an effect. But the majority of these trials have used a high dose of one antioxidant, vitamin E or beta carotene. In some studies with tocopherol or high doses of beta carotene adverse effects or undesirable results occur, probably because a single high dose of one compound is not efficient and may sometimes exert a pro-oxidant effect. In other cases, it was proposed that the population had a too low cardiovascular risk; secondary prevention trials were performed but did not show an improvement in CVD.

This lack of clinical efficacy does not disprove the oxidative hypothesis. It is possible that investigated antioxidants are not the right ones, that their dosage, formulation and bioavailability are not appropriate; that patient selection was inadequate and treatment length insufficient to provide full beneficial effects. For example, neither synthetic beta carotene nor tocopherol is equivalent to the natural form. Moreover plant-foods antioxidants are quite numerous in vegetables and fruits, and interact between them with synergistic effects.

So the proper approach should be to test the benefit of high intakes of plant foods naturally rich in antioxidant and folates such as fruit and vegetables in randomized trials on subjects having low intakes of these foods, and to stratify the subjects according to their level of oxidative stress (because antioxidant should be useful when diet fails to meet the global antioxidant and folate requirements), then to identify these subgroups which were more likely to benefit from these kinds of foods, and finally to start at the earliest stage of the disease. The final public health objective should be to modify the global diet and lifestyle.

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FRUIT AND VEGETABLE INTAKE AND BLOOD PRESSURE

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Increased fruit and vegetable consumption is associated with a decrease in blood pressure after several weeks

High fruit and vegetable intakes are associated with lower blood pressure in cross-sectional studies[1-4]. The decrease in blood pressure associated with the increase of fruit and vegetable intakes is shown in experimental studies[5-6].This decrease in blood pressure is observed after several weeks of dietary change and is maintained until the end of follow-up in experimental studies (6 months maximum).

In the DASH study[5] the systolic blood pressure (SBP) of 154 adults who were randomly assigned to eat a strict diet rich in fruit and vegetables decreased by 2.8 mm HG compared to the control group after 8 weeks. John et al[6] observed a decrease of 4 mm HG in subjects who were encouraged to increase their fruit and vegetable consumption to at least five servings per day after 6 months of follow-up. Experimental studies have shown that increased fruit and vegetable intakes in addition to other dietary behaviour modifications such as reduced sodium or increased dairy product consumption, also have an effect on blood pressure[7-9]. Theses results support the hypothesis that an increase in fruit and vegetable intake reduces blood pressure over a short-term period and this effect is maintained after several months of consumption.

Active components

Many components of fruit and vegetables are thought to be involved in the process of lowering blood pressure; the role of fibre[10], potassium, calcium and magnesium[11] has been confirmed in experimental studies. Results from intervention trials on vitamin or antioxidant supplementation effects are, however, less conclusive[12].

These results support the hypothesis that an increase in fruit and vegetable intake reduces blood pressure but since follow-up periods in experimental studies to date have been limited to only several months, less is known about the long-term effects of increased fruit and vegetable intake over a period of several years[13].

Could life-long high fruit and vegetable intake slow the rise of blood pressure (associated) with ageing?

The rise in SBP with age is a phenomenon observed world-wide[14]. However, very specific populations are not affected[15] by this increase, suggesting that environmental factors such as diet could be highly involved. Recently published[16-18] cohort studies suggest that fruit and vegetables could function as protective factors against this increase. In the Framingham Children's Study[16], children initially aged 3 to 6 years who ate more than 4 servings per day of fruit and vegetables had a comparatively lower increase in blood pressure by early adolescence: their mean SBP was 106 mm HG compared to 113 mm HG in the other children after a follow-up of 8 years. In the Chicago Western Electric Study[17], fruit and vegetables were associated with a lower increase in blood pressure in men initially aged 41 to 57 (in 1958) after seven years of follow up. In the SUVIMAX study (1995 to 2001) which included men and women aged 36 to 62 years at baseline, the increase in blood pressure was reduced by 2.2 mm HG in the highest quintile of fruit and vegetable consumers compared to the lowest quintile[18]. Fruit intake was also associated with a lower risk of incident hypertension in the CARDIA study[19].

Potential mechanisms of a long-term effect

The potential mechanisms of the long-term effects of fruit and vegetable intakes on the increase in blood pressure remain unclear and may be different than those involved in short-term decreases in blood pressure. In the SU.VI.MAX study, daily antioxidant supplementation was found to have no effect on the risk of hypertension[20] compared to placebo, suggesting that long-term changes in blood pressure may not be explained by antioxidant activity alone but by other fruit and vegetable components such as fibre. It is also likely that the negative association observed in cohort studies may be explained by confounding factors. For example, high fruit and vegetable consumers often have healthier behaviours which may not be completely controlled for when adjusting variables in observational studies. Only a long-term (several years or more) controlled trial could demonstrate the protective effects of fruit and vegetable intakes on blood pressure increases associated with ageing. This is hardly feasible with dietary interventions.

In conclusion, numerous studies recommend high fruit and vegetable intakes in order to have a protective effect on blood pressure.

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