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Commentary

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Vegetarian diet: panacea for modern lifestyle diseases?

M. SEGASOTHY and P.A. PHILLIPS[1]

From the Department of Medicine, Northern Territory Clinical School of Medicine of Flinders University, Alice Springs, and [1]Department of Medicine, Flinders University, Adelaide, Australia

Summary

We review the beneficial and adverse effects of vegetarian diets in various medical conditions. Soybean-protein diet, legumes, nuts and soluble fibre significantly decrease total cholesterol, low-density lipoprotein cholesterol and triglycerides. Diets rich in fibre and complex carbohydrate, and restricted in fat, improve control of blood glucose concentration, lower insulin requirement and aid in weight control in diabetic patients. An inverse association has been reported between nut, fruit, vegetable and fibre consumption, and the risk of coronary heart disease. Patients eating a vegetarian diet, with comprehensive lifestyle changes, have had reduced frequency, duration and severity of angina as well as regression of coronary atherosclerosis and improved coronary perfusion. An inverse association between fruit and vegetable consumption and stroke has been suggested. Consumption of fruits and vegetables, especially spinach and collard green, was associated with a lower risk of age-related ocular macular degeneration. There is an inverse association between dietary fibre intake and incidence of colon and breast cancer as well as prevalence of colonic diverticula and gallstones. A decreased breast cancer risk has been associated with high intake of soy bean products. The beneficial effects could be due to the diet (monounsaturated and polyunsaturated fatty acids, minerals, fibre, complex carbohydrate, antioxidant vitamins, flavanoids, folic acid and phytoestrogens) as well as the associated healthy lifestyle in vegetarians. There are few adverse effects, mainly increased intestinal gas production and a small risk of vitamin B_{12} deficiency.

Introduction

Lifestyle diseases such as obesity, diabetes mellitus, hyperlipidaemia, hypertension, coronary artery disease and cancer are common in industrialized countries. There is considerable epidemiological evidence suggesting that a vegetarian lifestyle is associated with a lower risk for these diseases. The beneficial effects could be due to the diet as well as the healthy lifestyle, which includes desirable weight, regular physical activity, and abstinence from smoking, alcohol and illicit drugs.[1] We have already reviewed the different types of vegetarian diets and their relevance to renal disease.[2] Briefly, vegetarian diets are lower in energy and their percentage of energy from fat and cholesterol, with higher fibre and folate content than a normal mixed diet. These result in lower body weight, blood pressure and plasma lipid levels than in omnivores. The vegetarian diet has beneficial effects on the renal haemodynamic response to protein, progressive renal disease, proteinuria and glomerulosclerosis, blood pressure and hyperlipidaemia in nephrotic syndrome. We now review the beneficial and adverse effects of vegetarian diets on primary hyperlipidaemia, diabetes mellitus, cardiovascular disease, stroke, dementia, neural-tube defects, age-related macular degeneration, gastrointestinal disease and cancer.

Address correspondence to Dr M. Segasothy, NT Clinical School of Medicine of Flinders University, Alice Springs Hospital, Box 2234, Alice Springs, NT 0871, Australia. e-mail: m.segasothy@nt.gov.au

Diabetes

Diets rich in fibre and complex carbohydrate and restricted in fat improve control of blood glucose concentration,[3] delay glucose absorption,[4] lower insulin requirements,[5] increase peripheral tissue insulin sensitivity,[6] decrease serum cholesterol and triglyceride values,[3,5] aid in weight control[7] and lower blood pressure in diabetic patients.[8] Studies using high-carbohydrate and high-fibre diets reported an average 40% reduction of insulin doses,[9–11] a 6–27% reduction in fasting serum glucose values[9,11] and a 10–32% reduction in serum cholesterol values.[9–11]

Cardiovascular disease

Studies have shown an inverse association between fruit, vegetable and fibre consumption and the risk for coronary heart disease. Inverse relations between vegetable consumption and myocardial infarction (odds ratio, OR, 0.79 for the highest tertile) and angina pectoris (OR 0.89) were seen in an epidemiological study of 46 693 subjects in Italy.[12] Two epidemiological studies suggest that frequent consumption of nuts may provide some protection against coronary heart disease. In the Adventist Health Study, which was a prospective cohort investigation of 31 208 Seventh-Day Adventists, subjects who consumed nuts more than four times per week, had fewer definite fatal coronary heart disease events (relative risk, RR, 0.52) and definite non-fatal myocardial infarction (RR 0.49), when compared with those who consumed nuts less than once per week. This was independent of traditional coronary risk factors such as blood pressure and relative weight, and other foods that were available for analysis, and was seen in both stratified and proportional hazards multivariate analyses.[13] The nuts consumed were peanuts (32%), almonds (29%), walnuts (16%) and other nuts (23%). In the Iowa Women's Health Study, 41 837 postmenopausal women were studied. Coronary mortality was inversely associated with nut intake in these women (RR 0.43 in women consuming nuts 2–4 times per week) after adjusting for multiple factors such as age, energy intake, body mass index, waist-hip ratio, presence of hypertension and diabetes, smoking status, use of hormone replacement therapy, alcohol intake, and level of physical activity and education.[14]

In a randomized, single-blind prospective interventional trial in 406 patients subjected to dietary intervention for 6 weeks, 24–48 h after acute myocardial infarction, a vegetarian diet resulted in significant decrease (34.5%) in total cardiac end points, including non-fatal (17 vs. 25) and fatal (8 vs. 12) acute myocardial infarction, and sudden cardiac death (4 vs. 7), compared to a control diet.[15] Complications such as angina pectoris, electrocardiographic changes after exercise, left ventricular hypertrophy, and ventricular ectopics (>8/min) were significantly decreased in the group eating a vegetarian diet, compared with those eating the control diet. After 1 year follow-up, cardiac events (non-fatal acute myocardial infarction, fatal acute myocardial infarction, and sudden cardiac deaths) occurred significantly less often in the intervention group than in the control group (50 vs. 82, $p<0.001$).[16] The mean age, sex, mean body weight, blood pressure, lipoproteins, risk factors, complications, electrocardiographic changes, initial level of cardiac enzymes, drug therapy and dietary intake (mean energy, total fat calories, polyunsaturated/saturated fat ratio, dietary cholesterol, fibre and salt) were similar in both groups at entry to the study.

In four patients who had severe angina pectoris, the angina resolved within 3–18 months on instituting a vegan diet. When the health of vegans and age- and sex-matched omnivore controls using the Cornell Medical Index was assessed, female vegans had fewer symptoms of cardiovascular disease.[17] In a short-term (24 days) study, stress management training (stretching/relaxation exercise and meditation) and a vegan diet produced improvements in 23 patients with ischaemic heart disease when compared with a non-intervention control group. There was a 44% mean increase in duration of exercise, a 55% mean increase in total work performed (bicycle ergometry), improved left ventricular regional wall motion and ejection fraction during exercise (exercise radionuclide ventriculography) and a 91% mean reduction in frequency of anginal episodes.[18] In two prospective randomized, controlled trials, 50 patients who were subjected to comprehensive lifestyle changes (low fat, vegetarian diet, stopping smoking, stress management training and moderate exercise) for 1 year showed significant overall regression of coronary atherosclerosis as measured by quantitative coronary arteriography. Degree of adherence was directly correlated with changes in percentage diameter stenosis. In contrast, patients in the usual-care control group showed significant overall progression of coronary atherosclerosis.[19,20] There were also reductions in the frequency (91%), duration (42%) and severity (28%) of angina in the experimental group. In contrast, control group patients reported a rise in frequency (165%), duration (95%) and severity (39%) of angina.[19] The design of the three studies[18–20] does not allow the determination of the relative contribution of each component of the intervention. There were significant reductions in total cholesterol (20.5–24.3%), LDL cholesterol (37.4%) and triglycerides (15.5%) in the intervention group compared to

the control group, suggesting a significant dietary contribution.

Stroke

Mortality from stroke has been declining for many decades in Europe and North America. This decline in mortality has been attributed to multiple factors, including the increased consumption of fruits and vegetables.[21] An inverse association between fruit and vegetable consumption and stroke has been suggested.[22–24] In a population-based longitudinal study of 832 middle-aged men over 20 years of follow-up, for each increment of three servings of fruit and vegetable per day, there was a 22% decrease in the risk of all stroke.[24] Similar results were observed for transient ischaemic attack and completed stroke, both ischaemic and haemorrhagic.

The protective effect of fruit and vegetables may be related to their potassium, antioxidant, α-linolenic acid and folate content, as well as their ability to lower serum cholesterol and blood pressure. The vegetarian diet has a blood-pressure-lowering effect.[2] Increased potassium intake may decrease risk of stroke by lowering blood pressure as well as by mechanisms independent of its effect on blood pressure, as indicated by animal studies.[25] The inverse association of low plasma carotene, vitamin C levels and vitamin C intake with risk of stroke,[26,27] and preliminary data from the Nurses' Health Study[28] both suggest a protective role for dietary antioxidant vitamins. A prospective study over 12 years involving 2974 middle-aged men in Switzerland showed that men with low plasma concentrations of both ascorbic acid and β-carotene had four times the risk of dying of stroke.[26] In a cohort study of 730 elderly men and women in the UK followed for 20 years, stroke among those in the highest tertile of vitamin C intake (mean >45 mg per day) was significantly reduced (RR reduction, RRR, 50%) compared to the lowest tertile (mean <28 mg per day). A similar gradient of risk was present for plasma ascorbic acid concentration (RRR 30%).[27] In 87 245 US female nurses, the RR of ischaemic stroke was 0.55 in women in the highest quintile of antioxidant vitamin score compared with those in the lowest. Carotene intake was the predominant contributor to the reduced risk, with modest contributions from vitamins C and E.[28]

Analysis of the Multiple Risk Factor Intervention Trial (MRFIT) suggests that higher levels of α-linolenic acid are independently associated with lower risk of stroke in middle-aged men at high risk for cardiovascular disease.[29] A standard deviation increase (0.13%) in the serum level of α-linolenic acid was associated with a 37% decrease in the risk of stroke ($p<0.05$). The role of folic acid will be discussed in the section on cardiovascular disease.

Although serum cholesterol is a major determinant of atherosclerosis, its role in the pathogenesis of stroke is unclear. However, recent trials of statins for secondary prevention of coronary artery disease have consistently shown that lowering lipid levels results in lower risk of stroke as well as coronary events.[30–32] Epidemiological studies indicate an inverse association between dietary intake of fat and saturated fat, and risk of stroke, supporting a beneficial effect.[33,34] The vegetarian diet, which includes fruits, vegetables, complex carbohydrates, soy bean, legumes, nuts and soluble fibre, could thus lower the risk of cardiovascular disease through multiple mechanisms such as lowering of cholesterol and the beneficial effect of antioxidant vitamins, folic acid, linolenic acid and fibre.

Mechanisms of cardiovascular prevention

At least part of the beneficial effects of vegetarian diet, with or without other lifestyle changes, probably results from a hypolipidaemic effect. In addition, vegetarian diets reduce weight and blood pressure, further improving primary and secondary prevention.

Soybean

Vegetable proteins are useful for the treatment of human hyperlipidaemia. A soy-bean-protein diet lowered the serum cholesterol to a greater degree than did a low-cholesterol, low-saturated-fat diet containing an equivalent amount of protein of animal origin.[35–37] Substantial decreases were observed in both serum cholesterol (21% after 3 weeks) and triglycerides, in patients with type IIa and IIb hyperlipoproteinaemia, including some with familial hypercholesterolaemia.[35,36] A recent meta-analysis of 38 human studies derived from 29 articles with a total of more than 740 subjects showed that the consumption of soy protein resulted in significant decreases in total cholesterol (0.60 mmol/l; 9.3%), low-density lipoprotein (LDL) cholesterol (0.56 mmol/l; 12.9%) and triglycerides (0.15 mmol/l; 10.5%).[38] There were no significant changes in high-density lipoprotein (HDL) cholesterol or very-low-density lipoprotein (VLDL) cholesterol concentrations. The magnitude of the lipid changes was greatest in those with the highest initial plasma cholesterol concentrations. Soy protein intake averaged 47 g per day. It was estimated that the ingestion of 25 or 50 g of soy protein per day could decrease serum cholesterol by 8.9%.[38] An intake of 30 g soy protein can be obtained by drinking two cups of soy milk and consuming one

serving of meat analogue. The mechanisms of the hypocholesterolaemic effect of soy protein are unknown. It has been suggested that the beneficial effect of soy may be the result of the amino-acid pattern and peptide structure of the soy protein[39] as well as from non-protein compounds such as isoflavones or phytoestrogens and saponins.[38–40]

Legumes

Leguminous seeds lower serum cholesterol in man.[41–44] Substitution of chick peas for wheat flour decreased serum cholesterol levels by 22% by the end of 55 weeks.[41] Consumption of 30 g dried legumes daily over a 3-month period resulted in a 16% decrease in serum cholesterol in hyperlipidaemia patients, compared to a 8.7% decrease in normal volunteers studied under similar conditions.[42] Substitution of about 140 g dried beans (kidney, pinto, chick pea, green and red lentils) daily for other sources of starch over a 4-month period in hyperlipidaemic patients resulted in a 7% decrease in total serum cholesterol and a 25% reduction in serum triglycerides. There were no significant changes in LDL and HDL cholesterol levels.[43]

Nuts

Nuts are rich in protein, monounsaturated fatty acids (oleic acid), vitamins (vitamin E, B_6, folic acid and niacin), minerals and fibre.[45] Walnuts are, however, rich in polyunsaturated fatty acids (linoleic and α-linolenic acids). Nuts are classified as part of the USDA Food Guide Pyramid's Meat/Meat Alternate Group and in the Mediterranean and Asian diet pyramids, have been placed on the same level as fruits, vegetables and legumes.[45]

Walnuts,[46,47] macadamia,[48] almonds,[47,49] and hazelnuts[46] have cholesterol-lowering properties, and a beneficial effect on the lipoprotein profile. In controlled, randomized, crossover study in 18 normocholesterolaemic men, diets rich in walnuts decreased total cholesterol (0.58 mmol/l; 12.4%), LDL cholesterol (0.47 mmol/l; 16.3%) and triglycerides (0.11 mmol/l; 8.3%). Although HDL cholesterol was lowered by 4.9%, the LDL cholesterol to HDL cholesterol ratio was lowered significantly by 12.0%. Likewise, a randomized controlled, crossover-designed study in 30 healthy subjects showed a macadamia-nut-based, high-monounsaturated-fat diet lowered serum total cholesterol and LDL cholesterol within 4 weeks.

Soluble fibre

Soluble fibres are abundant in fruits, dried beans, legumes, guar gums, barley, psyllium and oat cereals and can lower blood lipid levels.[50–52] A meta-analysis of 20 trials using oat products revealed that about 3 g per day of soluble fibre from oat products (28 g oat bran) can lower total cholesterol levels by 0.13–0.16 mmol/l, and the reduction is greater in those with initially higher blood cholesterol levels.[53] Oat bran is more effective in lowering cholesterol than wheat bran or oatmeal, as it contains more water-soluble fibre β-glucan.[54] A high intake of soluble fibre can further reduce plasma cholesterol even after marked reductions in dietary saturated fat and cholesterol have been achieved. A crossover study in 43 volunteers with hyperlipidaemia subjected to a metabolic diet high in soluble fibre, but low in saturated fat and cholesterol, demonstrated a fall in total cholesterol by 4.9% and LDL cholesterol by 4.8% during the soluble-fibre period.[55]

Calorie restriction

Vegetarian diets are lower in energy and percentage of energy from fat and cholesterol, and vegetarians have lower body weight than omnivores.[56–58] There is evidence that a low-energy diet can modulate blood lipids[59] and reduce atherosclerosis and coronary deaths,[60] and weight reduction may be associated with reduction in coronary artery disease and all its risk factors.[61,62] With a fat-modified diet, even modest weight reduction (4.5 kg) by obese people results in a 30% or 40% greater fall in the level of cholesterol than that resulting from the qualitative change in fat intake alone.[63,64] Weight reduction may also reduce cardiac enlargement, left ventricular strain, post-exercise electrocardiographic changes and arrhythmias,[61,65] possibly by reducing myocardial oxygen requirements and having other beneficial effects on cardiac indices.[62]

Antioxidant effects

The beneficial effect of vegetarian diet on cardiovascular disease could also be due to the presence of antioxidant vitamins such as vitamin E, vitamin C and β-carotene and flavanoids as well as folic acid, linolenic acid and fibre in fruits and vegetables. Oxidation of LDL cholesterol is an important step in the pathogenesis of atherosclerosis.[66] Vitamin E,[67] vitamin C,[68] β-carotene[69] and flavanoids[70] prevent the oxidation of LDL cholesterol. Four large prospective epidemiological studies found that high doses of vitamin E intake or supplementation were associated with a significant reduction in cardiovascular diseases.[71–74] The relative risk reductions (RRR) ranged from 31% to 65%. Studies involving β-carotene and vitamin C gave less consistent reductions in cardiovascular disease, the RRR ranging from -2% to 46%, and -25% to 51%, respectively.[71–73,75–77] Three other epidemiological studies have suggested

a role for flavanoids, especially quercetin, in the prevention of coronary artery disease.[78–81] However, all[82–89] but one[90] prospective randomized trial did not show reductions in cardiovascular disease with vitamin E, vitamin C or β-carotene supplementation. However, the prospective trials were designed to study cancer, not cardiovascular disease (fatal or non-fatal cardiovascular disease outcomes) and probably used suboptimal doses of vitamin E.[91] Furthermore, the prospective studies were of limited duration (usually a few years) and usually commenced in middle age when atherosclerosis may be well established, in contrast to epidemiological studies where intake is protracted (several years or decades) and started at a much younger age when the atherosclerosis is in the early stages.[91] Ongoing large-scale and planned long-term randomized trials designed specifically to evaluate effects on cardiovascular disease will help to resolve this controversy.

Folic acid and homocysteine

An elevated plasma homocysteine concentration is an independent risk factor for atherosclerosis of coronary, cerebral and peripheral vessels[92] and for deep-vein thrombosis.[93] One study found that 28–42% of patients with premature vascular disease had hyperhomocysteinaemia.[94] In the Physicians' Health Study, 14 916 male physicians were prospectively followed for about 5 years.[95] Men with plasma homocysteine concentrations that were 12% above the upper limit of normal had about a three-fold increase in the risk of myocardial infarction, as compared with those with lower levels, even after correction for other risk factors. A meta-analysis of 27 studies indicated that 10% of the risk of coronary artery disease in the general population is attributable to homocysteine.[96] An increase of 5 μmol/l in the plasma homocysteine concentration raised the risk of coronary artery disease by as much as an increase of 0.52 mmol/l in the cholesterol concentration.[96] A prospective study involving 587 patients with angiographically-documented coronary artery disease showed a graded association between plasma homocysteine concentrations and overall mortality.[97] In a cross-sectional study of 1041 elderly subjects in the Framingham Heart Study, high plasma homocysteine concentrations and low concentrations of folate and vitamin B_6 were associated with an increased risk of extracranial carotid artery stenosis.[98] There was a graded relation between plasma homocysteine and the risk of carotid stenosis. Likewise a graded increase in the relative risk of stroke with increasing serum homocysteine concentration was seen in a nested case-control study.[99] Total plasma homocysteine concentration was also found to be an independent risk factor for stroke and arterial thrombosis in patients with systemic lupus erythematosus.[100]

The predominant cause for elevated homocysteine blood concentrations is inadequate blood folate.[101] Folic acid supplementation has been shown to be highly effective in reducing plasma homocysteine levels.[96] Total homocysteine concentrations reach a reduced plateau when the folate intake approaches 400 μg/day.[101] It has been estimated that a folic acid increase of about 200 μg/day results in an average reduction of 4 μmol/l in total homocysteine concentration and an increase in folic acid intake of 350 μg per day in men and 280 μg per day in women would potentially prevent 30 500 and 19 000 deaths from vascular causes per year, respectively, in the US.[96]

Results from the Nurses' Health Study demonstrated a significant inverse relation between dietary intake of folate and vitamin B_6, and mortality and morbidity from cardiovascular disease during a follow-up of 80 082 women over a 14-year period.[102] The RR of coronary heart disease between extreme quintiles were 0.69 for folate and 0.67 for vitamin B_6 and 0.55 for both folate and vitamin B_6. The magnitude of the inverse association for folate was similar to their parallel study among male health professionals.[103] Each 100 μg/day increase in folate was associated with a 5.8% lower risk of coronary heart disease.[102] In a retrospective cohort study of 5056 men and women aged 35–79 years, there was a 69% increased risk of coronary mortality among those in the lowest quartile as compared with the highest quartile of serum folate.[104] In a small uncontrolled study of 38 patients with atherosclerosis of the carotid arteries, supplementation with folic acid, pyridoxine and vitamin B_{12} was associated with regression of plaque after a mean follow-up of 4.4 years.[105] Prospective, randomized, controlled trials will be necessary to determine the effect of folic acid supplementation on cardiovascular mortality.

Unsaturated fats

An inverse association between linolenic acid intake and coronary heart disease has been observed in several studies.[106–108] In 43 757 US health professionals followed-up for 6 years, intake of linolenic acid was inversely associated with risk of myocardial infarction.[107] The RR for a 1% increase in linolenic acid intake was 0.53 after adjustment for standard risk factors and intake of fibre, and 0.41 after further adjustment for intake of total fat. In a prospective secondary prevention trial, a Mediterranean α-linolenic-acid-rich diet was associated with lower cardiac deaths and non-fatal myocardial infarction.[108] The risk ratio for both these endpoints combined was 0.27. The incidence of coronary disease is low

in Japan, where the diet is rich in linolenic acid.[109] Foods rich in α-linolenic acid include green leafy vegetables, soybean products, grapeseed oil, canola oil, purslane, walnuts, hazelnuts and flax seed. The cardioprotective effects of α-linolenic acid may be due to its beneficial effects on platelet reactivity[110] and arrhythmia.[111]

Fibre

In a prospective cohort study of 43 757 US male health professionals followed-up for 6 years, the age-adjusted RR for total myocardial infarction was 0.59 among men in the highest quintile of total dietary fibre intake compared with men in the lowest quintile.[112] The inverse association was strongest for fatal coronary disease (RR 0.45). A 10 g increase in total dietary fibre corresponded to an RR for total myocardial infarction of 0.81. The main contributors for fibre intake were cereal (cold breakfast cereal), fruits (apples, bananas and oranges) and vegetables (peas, cooked carrots and tomato sauces). An inverse association between fibre and coronary disease has also been reported by previous smaller studies.[113–115]

In a new analysis of the Finnish α-tocopherol, β-carotene (ATBC) cancer prevention study in which 21 930 men were followed-up for 6 years, a high-fibre diet significantly reduced morbidity and mortality from coronary heart disease in middle-aged men who smoke.[116] For men in the highest quintile of total dietary fibre intake, the RR for coronary death was 0.69 compared with men in the lowest quintile of intake. A 10 g greater daily intake of fibre appeared to lower the risk of coronary death by 17%. Cereal fibre had a stronger association with reduced coronary death than vegetable or fruit fibre. In the food group analysis, intake of rye products, potatoes, vegetable and fruit were inversely associated with coronary death. The RR in the highest quintile of vegetable consumption compared with the lowest was 0.60. A 100 g greater daily intake of vegetables was associated with a 26% lower risk of coronary death.

Dementia

Cognitive impairment has been associated with lower vitamin C intakes and lower plasma ascorbic acid levels.[117–119] In 260 men and women aged >60 years in the US, those with low blood levels of vitamin C, folic acid, riboflavin or vitamin B_{12} had significantly lower scores on tests of memory and abstract thinking.[117] In 418 elderly men and women in China, low blood levels of vitamin C, riboflavin and folic acid were associated with low scores on the Hodkinson mental test.[118] In a 20-year follow-up study of 921 elderly men and women in the UK, cognitive impairment was associated with lower vitamin C intakes (OR 1.7) and lower plasma ascorbic levels (OR 1.6).[119] However, as these studies were cross-sectional, the lower vitamin C status could be a consequence rather than a cause of cognitive impairment. Low vitamin E levels were associated with dementia both in older people and in subjects with Down's syndrome.[120] In 341 patients with moderately severe Alzheimer's disease treatment with selegeline (10 mg/day) or α-tocopherol (2000 IU/day) for 2 years slowed the progression of disease.[121] The increase in median survival was 230 days for the patients receiving α-tocopherol, 215 days for those receiving selegeline, and 145 days for those receiving both, as compared with patients receiving placebo. These studies suggest that increased consumption of antioxidants such as vitamins C and E may delay cognitive impairment.

Age-related macular degeneration

Age-related macular degeneration is the leading cause of irreversible blindness in persons over the age of 65 years.[122] Serum levels of carotenoids have been significantly inversely related to the risk of age-related macular degeneration.[123] People with low intake of fruits and vegetables rich in vitamin A had a significantly higher risk for age-related macular degeneration compared with those whose consumption was high.[124] Adults in the highest quintile of carotenoid intake had a 43% lower risk of age-related macular degeneration, compared with adults in the lowest quintile of intake.[125] Among the carotenoids, lutein and zeaxanthin were most strongly associated with a reduced risk for age-related macular degeneration. Consumption of spinach and collard greens, which are rich in lutein and zeaxanthin, were associated with a dose-dependent reduction in risk of age-related macular degeneration. Lutein and zeaxanthin form the yellow pigment in the macula, and may prevent photic damage by absorbing blue light.[126] These pigments are found in green leafy vegetables, as well as fruits and vegetables of other colours such as maize, orange pepper, kiwi fruit, grapes, spinach, orange juice, zucchini and different kinds of squash.[127]

Gastrointestinal disease

Dietary fibre is protective against colorectal cancer. A review of 40 epidemiological studies described in 55 original reports indicated an inverse association between total dietary fibre intake and the incidence of colon cancer in 32 of the 40 studies.[128] These studies were performed on vegetarians as well as

non-vegetarians, and the main sources of fibre were fruits, vegetables, cereals, pulses and wheat.[128] Mechanisms for the inhibitory role of fibre in colorectal carcinogenesis include reducing faecal mutagen concentrations by increasing faecal bulk, reducing the exposure of colonic mucosa to faecal mutagens by reduced faecal transit time, and inhibiting faecal mutagen synthesis through fibre-induced changes in colonic pH or bacterial metabolism.[129] Fibre intake may influence colonic cell proliferation and the development of polyps in high-risk populations.[130]

There is an inverse relation between dietary concentration of cereal fibre and the prevalence of colonic diverticula, both in a lifespan study of rats[131] and in matched groups of vegetarians and non-vegetarians.[132] Vegetarians consuming 41.5 g fibre per day had an incidence of asymptomatic diverticular disease (12%) that was significantly lower than that in non-vegetarians (33%) who consumed 21.4 g fibre per day.[132] Dietary fibres shorten gastrointestinal transit time,[133] and increase stool weight,[134] frequency[135] and water content[135] thereby reducing constipation. An association between cholelithiasis and a diet low in protein, fat and crude fibre intake has been reported.[135] Intake of fibre is negatively associated with gallstones.[136] The fibre content of the diet influences bile salt metabolism and the concentrations of biliary lipids in bile.[137,138]

Cancer

Fibre and phytoestrogens

The protective role of dietary fibre against colorectal cancer has already been discussed. Epidemiological studies also suggest that the risk of breast cancer may be lowered by increasing the intake of dietary fibre and other dietary components associated with high intakes of whole grains, vegetables and fruits.[139] An inverse association between breast cancer risk and consumption of fibre and fibre-rich foods has been reported,[140,141] and there is a lower frequency of breast and prostate tumours in Asian countries, where soy foods, which are a rich source of fibre and phytoestrogens, are commonly consumed.[142] Five case-control studies of diet and breast cancer showed decreased cancer risk to be associated with high intake of soy bean products.[143–146] Three of the studies found a significantly reduced risk for premenopausal breast cancer[143–145] and one a reduced risk for postmenopausal breast cancer.[146] A case-control study showed that increased excretion of some phytoestrogens was associated with substantial reduction in breast cancer risk.[147] Colon cancer rates are low in Japan and China, where intake of soy bean products is high.[130]

Mechanisms by which fibre may aid in reducing breast cancer include lowering circulating levels of oestrogens.[148] Soy beans contain several classes of potentially important chemopreventing agents such as phytosterols, sitosterols, phytoestrogens, saponins, Bowman Birk inhibitor and chymostatin.[149] There are two principal varieties of phytoestrogens, namely isoflavones and lignans. Isoflavones genistein and diadzein are found predominantly in soy products,[150] whilst lignans are found in the fibre present in whole grains, berries, fruits, vegetables and flax seed.[151] Daily ingestion of soy protein lengthens the menstrual cycle and suppresses the usual midcycle surge in pituitary gonadotropins,[152] effects that are beneficial in decreasing risk of breast cancer. Phytoestrogens may exert an antioestrogenic effect by competing with estradiol for oestrogen receptors in breast tissue;[153] cell-culture studies and animal experiments show that they are tumour-inhibitory.[142] Animal studies also suggest that short-term exposure to dietary isoflavones neonatally or prepubertally decreases carcinogen induced breast cancer.[154] These studies suggest that the protective effect of the Southeast Asian diet occurs early in life,[155] and infants there are exposed to soy food early in childhood.

Antioxidants

Epidemiological studies indicate that people who consume higher dietary levels of fruits and vegetables have a lower risk of certain types of cancer[158] such as breast,[159] lung, oral, pancreas, larynx, oesophagus, bladder and stomach.[160] Certain subgroups of the American population, such as the Mormons and Seventh-day Adventists, who are vegetarians, have a significantly lower cancer rate.[161,162] The reduced risk of cancer associated with the consumption of fruits and vegetables has been postulated to be due to the presence of antioxidants such as vitamins E and C and β-carotene, and this has been well reviewed in many publications.[129,163–165]

Several correlational and case-control studies suggest that the consumption of vitamin C containing foods is associated with lower risk of certain cancers, particularly gastric, pancreatic, oesophageal, oral and laryngeal cancers.[129,163–165] Epidemiological, animal and clinical data suggest that vitamin E reduces oral carcinogenesis.[165] Supplementation with vitamin E has been reported to protect against lung cancer in non-smokers. Supplementation with vitamin E and β-carotene has been associated with a reduced prostate cancer incidence and mortality by one-third in men who smoke[167,168] and combined vitamin E, β-carotene and selenium supplementation decreased total mortality by reducing the rate of stomach cancer. The prevalence of esophageal cancer was

also reduced.[169,170] Epidemiological studies show that increased intake of vegetables, fruits and carotenoids and elevated blood levels of β-carotene are consistently associated with reduced risk of lung cancer.[156,157,171,172] Carotenoids may also reduce the risk of other cancers, such as breast, cervical, stomach and oropharyngeal, although the evidence is less extensive and consistent.[172] An inverse association between breast cancer and the total intake of vitamin A (preformed vitamin A and carotenoids) was seen in several case-control studies[173] and in one small prospective study.[174]

Recent long-term, large scale prospective trials, however, failed to demonstrate any beneficial effect of β-carotene and vitamin A, C, and E supplementation on cancer risk in populations with essentially normal intake,[159,167,175,176] and have raised concern about harmful effects of these antioxidants under certain conditions.[167,176] In addition, two smaller trials of β-carotene supplementation failed to demonstrate significant benefit in the prevention of recurrent skin cancer[177] and colon polyps.[178] The failure of supplementation with β-carotene and vitamins A, C and E to reduce cancer risk may be explained by these vitamins being markers for other nutrients present in fruits and vegetables. β-Carotene is one of 600 carotenoids that include lycopene, lutein and zeaxanthin, which are even more antioxidant than β-carotene in laboratory studies.[179] Similarly, there are many other plant compounds including more than 4000 flavanoids that may be responsible for beneficial (antioxidant) effects. The beneficial effects may be the result of a complex interaction between all the potential cancer-preventing substances (carotenoids, flavanoids, folic acid, vitamins A, C and E, selenium and fibre) in physiological doses rather than pharmacological doses of a single substance.

Adverse effects of vegetarian diet

The intake of vitamin B_{12} is lower in vegetarian diets[56,180] and deficiencies in this vitamin have been reported in vegetarians, especially vegans,[56,181] and in breastfed infants of vegans.[182–184]

Most vegetable oils are low in saturated fatty acids. Coconut, palm and palm kernel oil, in contrast to other vegetable oils, are rich in saturated fatty acids. Coconut and palm kernel oils are more saturated than animal fats; palm oil has similar proportions of saturated fatty acids to those of animal fats.[185] High intakes of saturated fatty acids have been associated with elevated plasma cholesterol levels, and concern has been expressed about the 'atherogenicity' of coconut and or palm oil in food products.[185]

Trans-unsaturated vegetable fats have adverse effects on cholesterol profiles, and could increase the risk of coronary heart disease.[186] The Health Professionals Follow-up Study[187] and the Alpha-Tocopherol, Beta Carotene Cancer Prevention Study[188] showed a RR for coronary heart disease of 1.4 and 1.39, respectively, for men in the upper quintile of dietary trans-fat intake. The Framingham Study found that after the first decade of follow-up, the RR of coronary heart disease was 1.1 for each additional teaspoon of margarine eaten per day.[189] The Nutrition Committee of the American Heart Association concluded that trans fat should be replaced when possible by monounsaturated or polyunsaturated oils in foods, because of its adverse effects on cholesterol profiles.[190]

Although serum cholesterol is a major determinant of atherosclerosis, there are conflicting reports of its role in the pathogenesis of stroke. Two ecological studies from Japan showed correlations between increased fat intake and decreased cerebrovascular mortality.[191,192] A cohort study of Japanese men living in Hawaii showed inverse association between total fat and saturated fat intake and all-stroke mortality.[33] In the Framingham Heart Study, which was a population-based cohort study, intakes of fat, saturated fat and monounsaturated fat but not polyunsaturated fat were associated with reduced risk of ischaemic stroke in men.[34] Low serum cholesterol has been shown to be a risk factor for haemorrhagic stroke.[193,194] These data imply that vegetarians have a higher risk for stroke as their intake of total fat and saturated fat is low, and their serum cholesterol level is low. However, a recent analysis of all published randomized trials of statin drugs showed that large reductions in cholesterol were associated with significant reductions in risk of stroke.[195]

The major side effects of vegetarian diets that are high in fibre and leguminous seeds is increased intestinal gas production, resulting in more flatulence and eructations.[43,189] Soy bean has a bland but somewhat beany aftertaste that may make it unappealing to Westerners.

Conclusions

A well-balanced vegetarian diet chosen from a wide variety of foods such as fresh fruits, vegetables, whole grains, cereals, nuts, seeds, legumes, beans and soy bean is rich in monounsaturated and polyunsaturated fatty acids (α-linolenic acid), minerals, fibre, complex carbohydrate, antioxidant vitamins [vitamins E, C and carotenoids (600; β-carotene, lycopene, lutein, zeaxanthin)], flavanoids (4000), folic acid and phytoestrogens, and is restricted in saturated fat. Substitution of plant sources of protein

for animal protein effectively decreases fat intake while increasing consumption of complex carbohydrate.

The burden of modern lifestyle diseases is enormous when the costs of investigation, diagnosis, treatment and primary and secondary prevention are included. Thus, dietary intervention with a vegetarian diet seems to be a cheap, physiological and safe approach for the prevention, and possibly management of modern lifestyle diseases. Ideally, it should be complemented with other healthy lifestyle practises such as regular exercise and abstinence from smoking, excessive alcohol and illicit drugs. Recognizing these benefits, the US Public Health Service has recommended a national dietary goal of increasing overall per capita consumption of fruits and vegetables in the American diet to at least five servings a day by the year 2000 to improve health and reduce disease risk.[197]

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