CHAPTER 2

Health Consequences of Vegetarian Diets

Populations consuming vegetarian and semi-vegetarian diets have lower rates of several chronic diseases that typically plague Western countries, including heart disease, hypertension, diabetes, and certain cancers. This is true of vegetarians living in Western countries and of populations consuming plant-based diets in developing countries. Migration studies indicate these differences are due to environmental factors. The incidence of heart disease and many cancers increases when people from countries where plant-based diets are consumed relocate to countries with diets predominantly based on animal products. Similarly, when people in developing countries become more affluent and begin to add more animal products to their diet, rates of chronic disease increase.[1,2]

Much of the available information about health effects of vegetarian diets comes from two large prospective epidemiologic studies. The Adventist Health Study (AHS)-1 is a cohort of 34,192 California Seventh-day Adventists (SDAs) that began in 1974–1976. The European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford) in the United Kingdom has 65,429 participants and oversampled for vegetarians. In addition, a second study of Adventists, the AHS-2, began in 2002 and had enrolled 96,194 participants as of 2007. It includes subjects from all 50 states and Canada and has provided some preliminary cross-sectional data based on enrollment questionnaires.

Smaller cohorts that also enrolled vegetarians were the Health Food Shoppers Study, the Oxford Vegetarian Study, both in the United Kingdom, and the Heidelberg Vegetarian Study in Germany.

Data from the AHS-1 showed that SDAs had longer life expectancies compared to the general population, which was attributable to a healthy lifestyle that includes exercise, tobacco avoidance, and healthful diet, and also that among the study participants, Adventist vegetarians had even greater life expectancy than nonvegetarians.[3] However, results from the EPIC-Oxford and the Oxford Vegetarian Study showed that, although British vegetarians were found to have low mortality rates compared to the general population, there was no difference in mortality between vegetarians and other study participants who had healthful lifestyles, although mortality from ischemic heart disease was 19% lower among the vegetarians.[4] Identifying precisely which dietary

factors affect disease rates of vegetarians is difficult because so many differences exist between vegetarians and nonvegetarians. It is therefore instructive to consider some of these dietary differences within the context of what is known about the relationship between specific dietary components and disease risk.

DIFFERENCES IN DIETARY COMPONENTS OF VEGETARIAN AND NONVEGETARIAN DIETS

Dietary Fat and Cholesterol

Differences in fat intake between vegetarians and nonvegetarians are not as striking as commonly thought. In the United States, fat intake has declined and now averages about 34% of caloric intake.[5,6] By comparison, lacto-ovo vegetarians and vegans consume diets that are 28–34% and 25–30% fat, respectively, although there is considerable variation among studies (Appendix A).

From studies involving direct comparisons (Appendix A; Table 2-1), it is clear that omnivores consume considerably more saturated fat than vegetarians, although both lacto-ovo vegetarians and omnivores consume more saturated fat than polyunsaturated fat. In contrast, vegans consume more polyunsaturated fat than saturated fat. Their lower saturated fat content is likely part of the explanation for the reduced rates of coronary heart disease (CHD) seen in some vegetarians and vegans, although recent research has raised some uncertainty about the relationship between saturated fat intake and CHD risk.[7]

Cholesterol intake is also lower among vegetarians. Data from the National Health and Nutrition Examination (NHANES)-III indicate average U.S. cholesterol intake is about 300 mg/d.[5] Lacto-ovo vegetarian cholesterol intake is typically between 150 and 300 mg/d, and strict vegan diets contain no cholesterol.

Dietary Fiber and Carbohydrate Intake

Fiber intake differs markedly between vegetarians and nonvegetarians. Older dietary surveys indicated that Americans consumed as little as 10 to 12 g of fiber/d,[8] but more recent data suggest fiber intake may be as high as 17 g/d for men and 16 g/d for women; these figures are more

Table 2-1 Comparison of Vegetarian and Nonvegetarian Intakes of Protein, Fat, Carbohydrate, Cholesterol, and Fiber

Nutrient	*Nonvegetarian*	*Lacto-Ovo Vegetarian*	*Vegan*
Fat (% total calories)	34	28–34	25–30
Cholesterol (total grams)	300	150–300	0
Carbohydrate (% total calories)	<50	50–55	50–65
Dietary fiber (total grams)	15–20	20–35	25–50
Protein (% total calories)	14–18	12–14	10–12
Animal protein (% total protein)	60–70	40–60	0

consistent with the data in Appendix A.[9,10] Nevertheless, lacto-ovo vegetarians generally consume between 50% and 100% more fiber than nonvegetarians, and vegans consume more fiber than lacto-ovo vegetarians. The U.S. Dietary Guidelines recommend 14 g fiber/1000 kcal.[11]

Not surprisingly, vegetarian diets are higher in carbohydrate than omnivore patterns. Vegans consume roughly 50–65% of their calories in the form of carbohydrate, lacto-ovo vegetarians about 50–55%, and omnivores generally <50% (Appendix A).

Protein

Protein accounts for approximately 15% of calories in the diet of Western omnivores. Americans typically consume 50–100% more than the adult protein recommended dietary allowance (0.8 g/kg body weight). Lacto-ovo vegetarians consume diets containing between 12% and 14% protein, and vegan diets are between 10% and 12% protein (Appendix A). Clearly, the type of protein consumed also differs. American omnivores derive about two thirds of their protein from animal foods; this has changed from the early 20th century when only half of dietary protein was derived from animal sources.[12] In contrast to the omnivore diet, about 40–60% of the protein in lacto-ovo vegetarian diets is derived from animal products, whereas vegans consume plant protein only.[13–15] In a sample of >6000 individuals who participated in the NHANES-III survey, Smit et al found that animal protein intake was directly associated with higher serum cholesterol levels even after controlling for saturated fat, fiber, and cholesterol intake, although it is extremely difficult to determine specific effects when variables are strongly collinear.[5]

Phytochemicals and Antioxidants

Antioxidants may reduce risk of a wide array of diseases, including arthritis, cancer, and heart disease,[16,17] although in recent years the importance of antioxidants has been called into question. Vegetarians consume higher levels of the three primary vitamin antioxidants: β-carotene and vitamins C and E. In addition, vegetarian diets are higher in phytochemicals (discussed later and in Chapter 8), many of which are potent antioxidants and may be protective against chronic diseases such as cancer and heart disease.

CARDIOVASCULAR DISEASE

In 1925, British physician Sir John McNee described to his colleagues two cases of atherosclerosis, a "rare disease" that he had observed while visiting the United States.[18,19] Today, slightly more than a third (34%) of Americans die of cardiovascular disease, although mortality rates have come down significantly since the mid-1960s. There are a number of reasons for this decline; lifestyle changes have contributed, but the widespread use of cardiopulmonary resuscitation and improved medical procedures are also very important factors.

Blood cholesterol levels in Americans have dropped somewhat in recent years and now average about 199 mg/dl.[20] Analysis of NHANES III data suggests that cholesterol levels have continued to decline, although the rate of decline has slowed in recent years.[21] Nevertheless, about 17% of the population have blood cholesterol levels that place them at high risk for heart disease (≥240 mg/dl), and another 30% have levels >200 mg/dl.[19] The biologically normal or

desirable level of blood cholesterol may be as low as 100 to 150 mg/dl.[22] Populations consuming traditional plant-based diets often have levels within this range.

Mortality rates from heart disease differ markedly throughout the world; in fact, the death rate due to heart attack is 10 times higher in some countries than in others. For example, in Shanghai, China, just 1 of every 15 deaths is due to heart disease.[23] Although genetic factors affect heart disease risk, they are unlikely to account for a substantial portion of this worldwide variation. Even within countries, differences in mortality rates clearly suggest an environmental influence; for example, rural Chinese have only half the rate of heart disease of urban Chinese.[24]

In a systematic review of cohort studies and randomized controlled trials (RCTs), Mente et al found that dietary factors strongly protective against CHD included vegetables, nuts, monounsaturated fat, and a Mediterranean-style diet, whereas factors that were strongly associated with increased risk were trans fats, high glycemic index, and a Western dietary pattern.[7]

Vegetarians and Heart Disease Risk

Nearly all studies in countries throughout the world show SDA and non-SDA vegetarian men have approximately half the risk of death due to ischemic heart disease in comparison to the general population.[25–33] Among SDAs, nonvegetarian men have a twofold to threefold increase in risk for CHD in comparison with vegetarian men.[33,34]

In an analysis of five prospective studies involving >76,000 individuals, death due to ischemic heart disease was 32% lower among vegetarian men compared to nonvegetarian men. Protective effects were greater in vegetarians who had followed their diet for at least 5 years and, interestingly, were greater at younger ages.[35] However, not all data are supportive of a protective effect of a vegetarian diet against CHD. In the Oxford Vegetarian Study, although heart disease rates were reduced >50% when compared to the general British population, meat eaters in this study had a lower risk than vegetarians.[29] Similarly, in a later analysis of this study, vegetarian diet was also not associated with a significantly reduced risk.[36]

A vegetarian diet also appears to be less protective against heart disease in women. In the combined prospective analysis just cited, death rates due to CHD were only 20% lower for female vegetarians versus 32% for men.[35] Consistent with this finding, in the AHS, beef consumption was associated with a more than twofold increase risk of fatal ischemic heart disease in men but was unrelated to risk in women.[37] Finally, in the AHS, vegetarianism was associated with a greatly reduced risk for heart disease among men but not among women.

Because smoking increases cardiovascular disease risk by approximately two- to threefold, the lower rates of heart disease seen in some studies may be due, in part, to avoidance of tobacco products. (Fewer than 5% of SDAs smoke.[38]) Even after controlling for smoking, however, several studies have found heart disease rates are still much lower among vegetarians.[26,28,32]

The lower incidence of hypertension among vegetarians, as discussed later, probably contributes to their reduced incidence of heart disease. Smokers who are hypertensive and hypercholesterolemic have 20 times the risk of heart disease of nonsmoking normocholesterolemic, normotensive men.[39]

It is well established that dietary pattern influences blood cholesterol levels and that high blood cholesterol increases risk for heart disease (Figure 2-1). As long ago as the early 1960s,

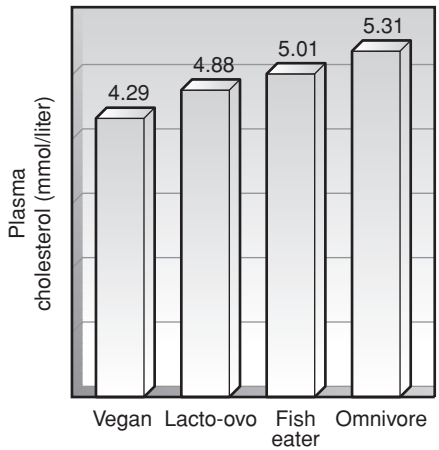

Figure 2-1 Effects of eating patterns on plasma cholesterol. Cholesterol values in vegans ($N = 114$), lacto-ovo vegetarians ($N = 1550$), fish eaters (lacto-ovo vegetarians who ate fish, $N = 415$), and omnivores ($N = 1198$). All groups included both men and women, but values were adjusted for age and gender. Average ages for each group ranged from 36 to 40 years. Cholesterol values for omnivores were significantly higher than for the other groups; values for fist eaters and lacto-ovo vegetarians were not significantly different from each other but were higher than those for vegans. *Source*: Data from Thorogood M, Carter R, Benfield L, et al. Plasma lipids and lipoprotein cholesterol concentrations in people with different diets in Britain. *BMJ*. 1978;295:351–353.

investigators observed that a vegan diet was effective in reducing angina in heart disease patients.[40] The lower heart disease rate and the lower blood cholesterol levels of vegetarians have prompted several investigators to examine the effects on blood cholesterol in subjects changing from a meat-based diet to a vegetarian diet. Not surprisingly, these studies have shown that adoption of a vegetarian diet lowers total cholesterol (TC).[41–48]

In 1991, the American Health Foundation in Valhalla, New York, concluded that a vegan diet could help both children and adults maintain low cholesterol levels.[49] The report found that, in comparison with omnivores, lacto-ovo vegetarians and vegans had blood cholesterol levels that were 14% and 35% lower, respectively. These findings were based on a review of only nine studies but are similar to those from the larger group of studies presented in Appendix B. More recently, a review of the health effects of 27 studies found significantly lower blood lipid concentrations among those following plant-based diets.[50] Vegetarians also had fewer and smaller age-related increases in circulating lipid levels.

In RCTs, plant-based and lacto-ovo vegetarian dietary interventions produce decreases in TC and low-density lipoprotein cholesterol (LDL-C) of about 10–15% compared to 15–25% for vegan diets.[50] Estimates suggest that a 1% decrease in cholesterol levels results in as much as a 2–4% decrease in risk[51,52] (Figure 2-2). Although vegetarians are leaner than omnivores and leanness results in lower TC levels, this is not the primary factor responsible for the lower cholesterol levels seen in vegetarians. In fact, Sacks et al found that, even when vegetarian subjects were

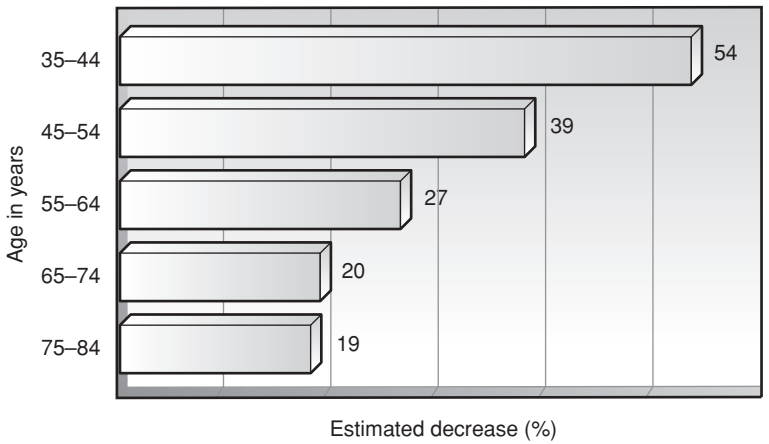

Figure 2-2 Percentage reduction in heart disease risk in men according to age associated with 10% decrease in blood cholesterol levels. The estimated decrease risk shown here for ischemic heart disease associated with a 0.6 mmol/liter (about 10%) decrease in serum cholesterol is based on findings of 10 prospective studies that involved approximately 500,000 men and 18,000 ischemic heart disease events. *Source*: Data from Cooper et al.[41]

heavier than a similar group of omnivores, plasma lipoprotein levels were still markedly lower among the vegetarians.[53]

Some studies, although not most, reported lower high-density lipoprotein cholesterol (HDL-C) levels in vegetarians in comparison with omnivores (Appendix B). In a review of the relationship between diet and lipoproteins, Knuiman et al concluded that replacing fat in the diet with carbohydrate lowers HDL-C levels.[54] In a study of 43 free-living men and women in England, switching from an omnivore diet to a self-selected vegetarian diet for 6 months caused HDL-C levels to decrease by an average of 21%.[55] However, Jenkins et al found that when carbohydrates were replaced with higher protein plant foods such as soy and nuts, the ratio of LDL to HDL cholesterol improved.[56]

Whether low HDL-C levels in vegetarians represent an increased risk for heart disease is the subject of debate.[57–59] Fraser noted that if low-fat diets equally decrease both LDL-C and HDL-C, this may explain why vegetarian diet is not protective, or is only modestly protective, against CHD in women because on a percentage basis, HDL-C is more protective against CHD in women than LDL-C is harmful.[60]

As discussed in Chapter 16, lower fat diets are often associated with higher serum triglyceride levels, which may increase CHD risk. However, in one intervention study using a very low-fat (10% of energy) vegan diet based on whole unprocessed plant foods, triglyceride levels decreased from a mean of 148.1 ± 16.1 to 120.02 ± 10.2 mg/dl.[61] Overall, though, studies indicate there is little if any difference in triglyceride levels between vegetarians and nonvegetarians. However, in many of those studies, total fat intake differed little between these two groups (Appendix B).

Other Factors Affecting Heart Disease Risk in Vegetarians

Protein

The higher polyunsaturated fat to saturated fat ratio of vegetarian diets compared to nonvegetarian diets primarily explains the decreased cholesterol level in habitual vegetarians and in omnivores adopting a vegetarian diet.[62,63] Nevertheless, there is some evidence, albeit weak, that meat protein, independent of dietary fat, may increase cholesterol levels. For example, subjects who consumed a 30% fat diet that included lean meat experienced only half the reduction in TC compared with subjects who consumed a lacto-ovo vegetarian diet and similar amounts of total fat, saturated fat, and cholesterol.[64] Also, data from the NHANES-III show animal protein intake is directly associated with higher serum cholesterol levels even after controlling for several other dietary factors known to affect blood cholesterol.[5,65]

However, most studies that have found animal products to be associated with an increase in blood cholesterol have concluded that the elevated cholesterol results from their fat and cholesterol content and not protein content.[62,66,67] In general the effects, if any, of protein type on cholesterol levels are probably minor, although there are important exceptions. Even soy protein, which was granted a health claim by the U.S. Food and Drug Administration in 1999, lowers LDL-C by only 3% or 4%[68] (Chapter 9). However, Jenkins et al have shown that a low-carbohydrate, high vegetable-protein diet was more effective than a similar diet using animal protein in reducing LDL-C and apolipoprotein-B.[56] In addition, these investigators have shown that a comprehensive dietary approach to lowering cholesterol can result in reductions of LDL-C by as much as 30%.[69]

Fiber

Soluble fiber has been shown to lower blood cholesterol levels. A pooled analysis of data from 10 prospective cohort studies found that higher fiber intake was associated with reduced risk of all coronary events.[70] And, in the EURODIAB IDDM Complications Study, which involved nearly 2000 participants, higher fiber intakes were independently related to beneficial alterations in serum cholesterol levels in both men and women with type 1 diabetes.[71]

Glore et al found that in 68 of 77 studies reviewed, soluble fiber decreased blood cholesterol by an average of about 10%.[72] However, other estimates suggest that the effects of fiber on cholesterol are more modest. For example, a meta-analysis that included 67 controlled trials found that whereas insoluble fiber had little effect, soluble fiber at levels that can reasonably be consumed (3 g/d) lowered LDL-C by about 5 mg/dl.[71,73] In addition to lowering cholesterol, increasing dietary fiber has been shown to inhibit the rise in triglyceride levels that often occurs with low-fat diets.[74,75]

In regard to fiber and CHD rates, in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, for men in the highest quintile of total dietary fiber intake (median, 34.8 g/d), the relative risk (RR) for coronary death was 0.69 (95% confidence interval (CI), 0.54 to 0.88; $P < 0.001$ for trend) compared with men in the lowest quintile of intake (median, 16.1 g/d) after controlling for a host of cardiovascular risk factors. Soluble fiber was slightly more strongly associated with reduced coronary death than insoluble fiber.[76] In agreement, a prospective study involving

male health professionals found that a 10-g increase in total dietary fiber corresponded to an RR for total myocardial infarction of 0.81 (95% CI, 0.70 to 0.93).[77] Furthermore, cereal fiber was most strongly associated with a reduced risk of total myocardial infarction (RR, 0.71; 95% CI, 0.55 to 0.91 for each 10 g/d increase in cereal fiber).[77] And finally, based on data from four studies, high intakes of whole grains were associated with a significant 26% reduction of risk for ischemic strokes.[10] The higher amounts of fiber consumed in these prospective and cross-sectional studies are similar to those consumed by vegetarians.

Phytochemicals

As discussed in Chapter 8, phytochemicals may exert a multitude of biologic effects, although much of the support for the beneficial effects of phytochemicals is based on in vitro and animal data or on the beneficial effects associated with fruit and vegetable consumption in epidemiologic studies.

In regard to cholesterol reduction, several phytochemicals have been investigated, but phytosterols, in particular, have received much attention during the past 15 years. A health claim for the cholesterol-lowering effects of phytosterols was approved by the U.S. Food and Drug Administration in 2000. Phytosterols, when consumed in amounts ranging from 1 to 2 g/d, lower serum cholesterol levels approximately 10%, even in normocholesterolemic subjects.[78] Vegetarians and people consuming plant-based diets consume considerably more phytosterols than omnivores, but intake is still no more than 500 mg/d.[79–82] Interestingly, Howell et al concluded that the higher phytosterol content of polyunsaturated oils partially explains the ability of these oils to lower serum cholesterol to a greater extent than olive oil, which is low in phytosterols.[83] Also, in a controlled feeding study, Racette et al found that approximately 500 mg of phytosterols lowered LDL-C about 5%, although the results were not quite statistically significant.[84]

Antioxidants and Pro-oxidants

The high antioxidant content of vegetarian diets may reduce heart disease risk, although this is quite speculative. Clearly many heart attacks occur in people with normal or only mildly elevated cholesterol. In fact, although smoking, high blood cholesterol, and high blood pressure are major risk factors for heart disease, these three risk factors may predict only about 30% of all cardiovascular events.[85] The role of antioxidants in preventing atherosclerosis remains unclear,[86] but the oxidation of serum lipoproteins appears to be a factor in atherosclerosis. Some findings suggest that only oxidized LDL-C is taken up by macrophages that are found within the intima, the innermost layer of the arteries.[87] Also, only nonoxidized HDL-C is thought to remove cholesterol from deposits along the walls of the arteries.[88]

The primary antioxidant nutrient thought to protect LDL-C from oxidation is vitamin E, but vitamin C may also have an important role by helping regenerate the reduced form of vitamin E.[89–92] Vegetarians have higher blood levels of both vitamins E and C, and, not surprisingly, the molar ratio of vitamin E to cholesterol in LDL-C is higher among vegetarians than omnivores.[93–96] Serum levels of β-carotene are also higher in vegetarians, and limited data suggest carotenoids may reduce CHD risk.[97,98] In one study, vegetarians ($n = 31$) had approximately 15% higher levels of plasma carotenoids compared to omnivores ($n = 58$), including lutein, α-cryptoxanthin,

lycopene, α-carotene, and β-carotene.[99] However, among vegetarians in Slovakia, differences in levels of antioxidants were seen in older but not younger vegetarians.[100] Despite initial promise, recent clinical studies evaluating the coronary benefits of vitamin E have proven disappointing.[101,102] Although results of RCTs have been unsupportive of a role for either vitamin E or β-carotene, large prospective cohort studies provide evidence for a protective effect of a diet high in carotenoid-rich fruits and vegetables.[103]

In vitro, β-carotene has been shown to inhibit the oxidation of a lipoprotein(a) (LPA; a modified form of LDL-C).[104] LPA is an independent risk factor for CHD.[105] In one study, serum LPA levels in female vegetarians were 45% lower than in a similarly matched group of omnivores.[106] The lower saturated fat and cholesterol intake of vegetarians may also act to reduce LDL-C oxidation.[107] Finally, and of particular interest, is the finding that dietary cholesterol increases LDL-C oxidation; therefore, it may be through this mechanism that dietary cholesterol increases CHD rather than by increasing serum cholesterol levels.[108]

In addition to nutrients, there is a wealth of information indicating that many of the main dietary phytochemicals (discussed in Chapter 8) are potent antioxidants, in some cases, much more so than vitamins C or E. Phytochemicals, even more so than nutrients, may play a protective role against CHD.[109] Several studies have found that flavonoid intake is associated with a reduced risk of CHD.[110–114] Flavonoids are potent antioxidants and widely distributed among fruits and vegetables, and they are also found in wine. In fact, the flavonoid content of red wine may play a role in the French paradox, the relatively low rate of heart disease in France compared with other Western countries with similar intakes of saturated fat,[115] although the concept of the French paradox has been challenged.[116]

Antioxidant Status

Evidence that the antioxidant status of vegetarians is superior to that of their nonvegetarian counterparts is somewhat equivocal. For example, although Nagyová et al failed to find in vitro conjugated diene (a measure of oxidation) formation in LDL-C isolated from vegetarians differed from that of nonvegetarians, they did find that vegetarians' LDL-C was more resistant to oxidation on the basis of thiobarbituric acid–reacting substances and also that the total antioxidant status of vegetarians was greater than in nonvegetarians.[94] The latter finding agrees with many, but not all, studies.[95] Vegetarians also have higher blood catalase activity and lower levels of conjugated dienes in comparison with omnivores.[117] In regard to intervention studies, the consumption of a vegan diet (in combination with walking) was shown to markedly reduce serum peroxide levels[118] and to lower concentrations of lipid peroxides.[119,120]

Some evidence suggests that iron may increase heart disease risk because it can act as a prooxidant, thereby increasing LDL-C oxidation.[121,122] Therefore, the lower iron stores seen in vegetarians (Chapter 6) may be an additional factor in reducing heart disease risk. Harvard University researchers found that the intake of heme iron, but not nonheme iron, was associated with a marked increase in heart disease risk.[123] However, they found that blood donation, which would result in lower iron stores, was not associated with a lower risk of CHD in men.[124] Furthermore, in a systematic review of prospective studies, Danesh and Appleby concluded there was no association between iron status and CHD risk.[125] Controlled feeding studies have also failed to support

this relationship.[126] Therefore, it is not clear if the combination of the higher intake of antioxidants and the lower iron stores of vegetarians work to inhibit LDL-C oxidation and to reduce heart disease risk. Interestingly, higher iron stores have been associated with increased insulin resistance,[127] which could increase risk of developing diabetes and thereby indirectly increase risk of heart disease.

Homocysteine

Some research has suggested that increased serum levels of the amino acid homocysteine are an independent risk factor for vascular disease.[128,129] In 1995, Boushey et al, on the basis of a meta-analysis that included 27 studies, concluded that about 10% of coronary artery disease was attributable to elevated homocysteine levels and that a 5 mmol/liter homocysteine increment elevates coronary artery disease risk as much as an increase in cholesterol of 20 mg/dl.[129] However, several recently conducted RCTs using homocysteine-lowering therapies failed to show any benefit in patients with prior stroke or coronary artery disease[130,131–133] or in patients without preexisting cardiovascular disease.[134] Thus the link between circulating homocysteine levels and risk of CHD has been called into question.

Low serum levels of folate, vitamin B_{12}, vitamin B_6, and riboflavin are associated with high homocysteine levels. When folate intake is adequate, vitamin B_{12} appears to be an important determinant of homocysteine levels. The connection between vitamin B_{12} and homocysteine may explain why several studies,[135–142] but not all[143,144] have found that serum homocysteine levels are higher in vegetarians than nonvegetarians (Figure 2-3). Furthermore, vitamin B_{12} injections were shown to lower serum homocysteine levels in a group of vegetarians, many of whom had abnormally low vitamin B_{12} and high homocysteine levels at baseline.[145] Thus the poorer vitamin B_{12} status of many vegetarians appears to increase homocysteine levels, countering the possible homocysteine-lowering effects of the higher folate intake. As previously noted, the clinical implications if any of these possibly higher levels are unclear. However, among Taiwanese postmenopausal women, low LDL-C levels in the vegetarians were not associated with differences in carotid atherosclerosis, a finding that may have been attributable to their higher levels of homocysteine.[146]

Factors Affecting Platelet Aggregation

Many CHD risk factors, aside from the most discussed ones such as elevated blood pressure and cholesterol, are affected by diet and may affect CHD in vegetarians. These include high fibrinogen levels,[147] increased platelet aggregation,[148,149] and elevated serum and tissue concentrations of certain prostaglandins. Dietary fat, and saturated fat in particular, increases factor VII levels, which increases platelet aggregation[150–152] Thus vegetarian diets may favorably affect these processes because they are lower in both total and saturated fat.

No clear picture emerges in regard to vegetarian diet and platelet aggregation, however. In a study of fibrositis/fibromyalgia patients placed on a vegetarian diet, fibrinogen levels decreased after 3 weeks.[153] However, although Ernst et al[154] found that vegetarians had reduced blood viscosity, vegetarians in this study and in other studies[155–158] did not have lower fibrinogen levels. Furthermore, in several studies no differences in platelet aggregation were noted between vegetarians and omnivores[156,157,159,160] In fact, one study found that, contrary to expectation, vegetarians

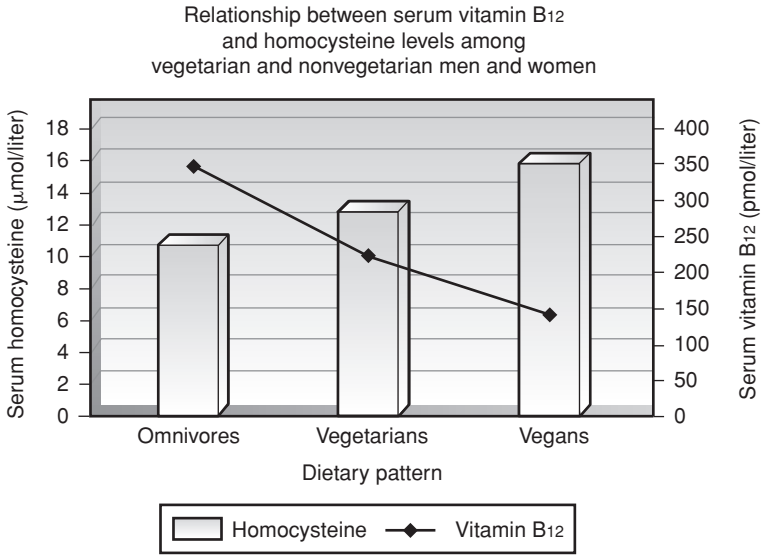

Figure 2-3 Inverse relationship between serum vitamin B_{12} and homocysteine levels: $N = 59$ omnivores, 54 vegetarians, and 32 vegans.

had a significantly higher platelet aggregation in comparison to meat eaters,[158] although this study disagrees with that from another group of researchers.[145]

Specific Fatty Acids and Heart Disease

Unsupplemented vegetarian diets generally do not contain the long-chain polyunsaturated n-3 (omega 3) fatty acids EPA and DHA or may contain only small amounts if sea vegetables and eggs are regularly consumed. The plasma concentrations of EPA and DHA have been found to be lower in vegetarians than in omnivores in some studies.[106,136,161,162] These fatty acids, which are found predominantly in certain types of fish, may have a role in reducing chronic diseases such as heart disease, via their conversion into the n-3 series prostacyclins and thromboxanes, which can favorably affect physiologic processes such as platelet aggregation. In contrast, vegetarian diets can be high in the essential fatty acid, linoleic acid, an n-6 fatty acid that can serve (via arachidonic acid) as a precursor to the n-2 series prostacyclins and thromboxanes. Also, linoleic acid competitively inhibits the conversion of the n-3 fatty acid, α-linolenic acid, which vegetarians do consume, into EPA and DHA, thereby decreasing the synthesis of the n-3 series prostacyclins and thromboxanes. The relationship of fatty acids to heart disease is discussed in considerable detail in Chapter 4.

Specific Foods

Certain foods that are commonly consumed by vegetarians may play a role in reducing risk for heart disease. Soyfoods are believed to reduce cholesterol levels due to both their protein and

Exhibit 2-1 Factors Common to Vegetarians That Are Thought to Reduce Coronary Heart Disease Risk

• Lower saturated fat intake	• Higher phytochemical intake
• Lower cholesterol intake	• Higher folate intake
• Lower heme iron intake	• Lower iron stores
• Higher fiber intake	• Lower body mass index
• Higher antioxidant intake	• Lower blood pressure

isoflavone contents (Chapter 9). Tree nuts are frequently an important part of vegetarian diets, particularly those of SDA vegetarians and have been shown to reduce serum cholesterol levels with decreases greater than predicted from their fatty acid content.[163–166] Exhibit 2-1 summarizes the factors in vegetarian diets that may reduce heart disease risk.

HYPERTENSION

In the United States, nearly 30% of adults have hypertension.[167] There are striking differences in blood pressure among populations worldwide. In industrialized societies, blood pressure typically increases with advancing age, and the prevalence of hypertension is high. Migrant studies demonstrate an environmental influence on blood pressure in that blood pressure rises in children and adults after they move from indigenous cultures to areas having a diet and lifestyle more characteristic of economically developed societies. Also, in some agrarian societies, sizable age-related blood pressure changes do not occur in most adults, and the prevalence of hypertension among the elderly remains low.[168]

Interest in the possible blood pressure–lowering effect of a vegetarian diet dates back to 1917 when Hamman concluded that meat was harmful for patients with hypertension.[169] Subsequently, in 1926, Donaldson reported that blood pressures of vegetarian college students increased significantly within 2 weeks of adding meat to their diet.[170] Four years later, Saile reported that German vegetarian monks had lower blood pressures at all ages than monks who ate meat.[171] About that same time, Heun observed a mean decline in systolic blood pressure of 60 mm Hg and a decrease in diastolic blood pressure of 28 mm Hg in 14 severely hypertensive patients who were treated with a fruit and vegetable diet.[172] These observations are consistent with studies showing that vegetarian Buddhist monks did not experience the rise in blood pressure with age seen in omnivore controls matched for age, sex, and body mass index (BMI) and that the duration of vegetarianism was inversely related to blood pressure.[173,174]

Appendix C lists studies in which blood pressure in vegetarians was compared with that in omnivores (see also Figure 2-4). In many of these studies vegetarians had both lower systolic and diastolic blood pressure. Although differences between vegetarians and omnivores were generally between 5 and 10 mm Hg, this degree of difference may have a significant impact on morbidity or mortality. In 55- to 59-year-old men, a reduction in systolic blood pressure of only 5 mm Hg has been estimated to result in a 7% reduction in major coronary events.[175] Similarly, a reduction

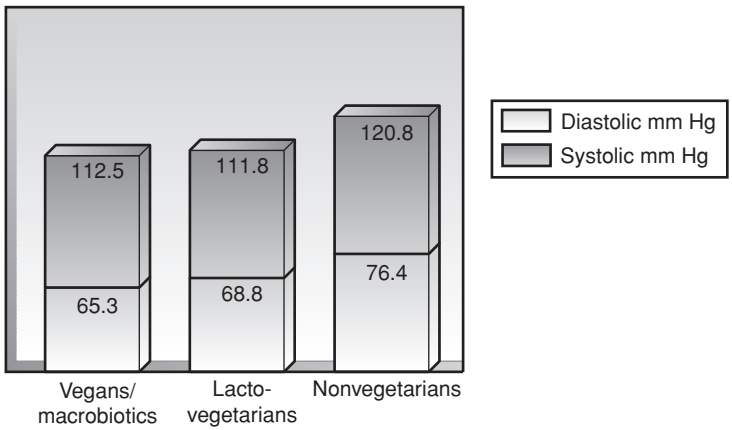

Figure 2-4 Differences in blood pressure between vegetarians and meat eaters. There were 226 vegans (macrobiotics), 63 lacto vegetarians, and 458 nonvegetarians. The vegans and lacto vegetarians had adhered to their dietary patterns for approximately 2 and 3 years, respectively. The systolic and diastolic blood pressures of both groups of vegetarians were significantly lower than those of the omnivores ($P < 0.0001$), and the diastolic pressure of vegans was significantly lower than that of the lacto vegetarians ($P < 0.02$). Significant differences between vegetarians and nonvegetarians existed after controlling for body weight. *Source*: Data from Sacks et al.[184]

in blood pressure of only 4 mm Hg was found to cause a marked reduction in mortality from all causes in the Hypertension Detection and Follow-Up Program.[176] Also, differences in blood pressure between vegetarians and nonvegetarians were likely minimized because of the selection criteria for study subjects.

Not only is average blood pressure lower in vegetarians, but the extent of actual hypertension appears to be lower as well. In the AHS-1, nonvegetarian men and women, and semi-vegetarian men and women, were more than twice, and about 50% more likely, respectively, to be hypertensive than vegetarians.[37] Preliminary results from the AHS-2 show lower rates of hypertension among vegetarians and show that vegans have less hypertension than other vegetarians.[177]

An analysis of a prospective epidemiologic study that included 11,004 British subjects showed that omnivore men were >2.5 times as likely as vegan men to have hypertension.[178] Ophir et al reported that 42% of the nonvegetarians studied had hypertension (140 mm Hg/90 mm Hg) compared with only 13% of the vegetarians.[179] The prevalence of blood pressure >160/95 was 13 times higher in the nonvegetarians (26% vs 2%).[179] In another study, 37% of the nonvegetarians but only 14% of the vegetarians had a history of physician-diagnosed hypertension.[180] Similarly, the prevalence of hypertension requiring current medication use was 44% and 22% among African American and white nonvegetarian subjects, respectively, but only 18% and 7% among African American and white vegetarians.[181]

There is conclusive evidence that dietary changes can significantly lower blood pressure.[182] For example, in the Dietary Approaches to Stop Hypertension (DASH) trial, a low-fat diet that was

high in fruits, vegetables, and calcium was associated with reductions in blood pressure that were similar to those expected from blood pressure medication.[183,184] Even in subjects with high normal blood pressure, blood pressure declined by 3.5 mg Hg in response to the combination diet. Furthermore, reductions in blood pressure were achieved without any changes in sodium intake.

Obesity is positively related to blood pressure, whereas regular exercise and weight loss tend to lower it.[185–189] In the Nurses' Health Study, obesity and weight gain during adulthood were both related to higher blood pressure. Gaining just 20 pounds since the age of 18 years doubled the chances of having high blood pressure during midlife, whereas losing about 20 pounds reduced the risk of having high blood pressure by about 25%.[190]

Nevertheless, in most studies that found blood pressure to be lower in vegetarians, weight was controlled for, and in two where it was not, weight differences were thought to have little if any impact[191,192] Ophir et al found that the blood pressure of nonvegetarians is appreciably higher than that of vegetarians with similar body weights.[179] Only when subjects were obese (i.e., >20% of the average weight) were no differences in blood pressure seen between vegetarians and nonvegetarians. However, the results of these studies contrast with those from the EPIC-Oxford Study, which showed that most of the difference in blood pressure between vegans and omnivores was explained by differences in BMI.[178]

Although exercise helps reduce blood pressure, Rouse et al found that Mormon women had higher blood pressures than SDA women, even though the Mormons exercised more.[193] For men, there were no differences in the frequency of activity among Mormon omnivores, Adventist omnivores, and Adventist vegetarians, but the vegetarians had the lowest systolic blood pressure.

Rouse et al were the first to clinically evaluate the effects of a vegetarian diet on blood pressure.[42] They found that systolic and diastolic blood pressures decreased by about 6 and 2 mm Hg, respectively, when normotensive omnivore subjects were placed on a lacto-ovo vegetarian diet. In a later study involving a similar design, mean systolic and diastolic blood pressures decreased 6.8 and 2.7 mm Hg, respectively, on a lacto-ovo vegetarian diet.[194] Other studies have also reported hypotensive effects of a vegetarian diet in normotensive subjects,[195] mildly hypertensive subjects,[196] and hypertensive subjects.[43]

Several studies have tried to determine the dietary component of vegetarian diets that is responsible for their hypotensive effect, but the absence of neither meat[197,198] nor milk protein[199] appears to be a contributing factor. However, studies suggest that increased plant protein intake may be associated with lower blood pressure[200,201] and that replacing carbohydrate with either protein or monounsaturated fat could reduce blood pressure as well. Furthermore, in a prospective study of 2895 adults, a lower intake of nonheme iron at baseline was associated with higher systolic blood pressure and pulse pressure at 5.4-year follow-up.[202] Among French adults, higher fiber consumption was associated with lower blood pressure.[203] Differences in potassium, magnesium, and calcium[42] or vitamin C appear to be too small to account for the observed blood pressure differences.[204] Although blood pressure in agrarian societies with primarily vegetarian diets and low sodium intakes is lower than in industrialized nations, the sodium intake of vegetarians in industrialized countries is similar to, or only modestly lower than, that of omnivores (Appendix G). Thus sodium intake does not appear to be the explanation for blood pressure differences between omnivores and vegetarians.

The lower glycemic index typical of vegetarian diets has been suggested as one possible explanation for lower blood pressure in vegetarians.[205] The lower blood pressure of vegetarians may be

partly affected through a blood glucose-insulin sympathoadrenal mechanism, as postulated by Landsberg and Young.[206] They suggested that the lower blood pressures of vegetarians may be related to the slower delivery of glucose to the blood as a result of an increased consumption of complex carbohydrates and a decreased sucrose intake. Sacks and Kass suggested that modest intake of animal products may be a marker for a large intake of other potentially beneficial nutrients from vegetable products that collectively have a hypotensive effect.[207] It is almost certain that it is the combination of dietary changes incurred when changing to a vegetarian diet that elicits the blood pressure–lowering response, rather than just one or two dietary factors.[189,204,208–210]

CANCER

There are striking dissimilarities in cancer rates among countries and geographic regions. Although genetic differences among populations may contribute to international variations in cancer rates, the evidence that lifestyle-related factors are important is persuasive and is based on migration studies, intracountry variations, and trends within countries. Migration data also suggest that, at least for some cancers, events that occur late in life markedly influence cancer mortality.[211] Thus dietary interventions in adulthood hold the potential to reduce cancer risk.

In most respects, vegetarian diets, because of their lower fat and higher fiber content, are closer to matching the dietary guidelines issued by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) than typical American eating patterns. Vegetarians may also achieve the cornerstone of dietary guidelines aimed at reducing cancer risk-to increase fruit and vegetable consumption. Epidemiologic data support the anticancer effects of fruits and vegetables, although not all studies support this relationship.[212,213] The proposed biologic mechanisms for these protective effects include enhanced antioxidant activity, increased levels of detoxification enzymes, regulation of cellular growth factors,[214,215] and modulation of steroid hormones and metabolism.[216]

Only limited data are available, however, on vegetarian fruit and vegetable intake, although data from the Continuing Survey of Food Intake by Individuals confirmed that vegetarians had higher intakes of fruit and vegetables than nonvegetarians,[217] as did a study of dietary habits of Swedish vegans.[218] Also, a study of 35,367 British women taking part in the UK Women's Cohort Study found that being a vegetarian was among the strongest predictors of a high fruit and vegetable intake.[219] Nevertheless, the simple elimination of meat and/or dairy products from the diet does not necessarily lead to greater fruit and vegetable intake because these foods are typically not used as replacements for animal foods. It is more likely that the greater health awareness of vegetarians results in their higher fruit and vegetable intake.[220–225]

Furthermore, in recent years, evidence in support of the protective effects of plant-based diets has arguably not been as strong as was anticipated. For example, in their comprehensive review of the diet and cancer literature, published in 2007, the WCRF/AICR concluded that the evidence that fruit and vegetable intake reduces cancer risk is not as strong as it was a decade earlier.[226] However, they also emphasized consumption of more plant foods and less meat, especially processed meat, as a means of decreasing cancer risk.

Establishing the relationship of diet to cancer is difficult because of the lack of noninvasive or minimally invasive intermediary markers for cancer risk. In contrast, serum cholesterol and blood

pressure are confidently viewed as indicators of CHD risk, and both respond fairly rapidly to dietary change and can be easily measured in humans. Some cancer markers do exist, such as prostate-specific antigen levels for prostate cancer and breast tissue density for breast cancer, but each of these carries with it important limitations. Another limitation is that early life events (even those that occur in utero) may play a particularly important role in the etiology of certain cancers.[211] This may especially be the case for breast cancer.[211,227] For example, there is substantial evidence that modest soy consumption during childhood and/or adolescence markedly reduces adult breast cancer risk (Chapter 9).[228] Because epidemiologic studies typically obtain recent dietary intake data from older adults, they may miss important links between diet and cancer risk.

The cancer process is extremely complex and likely affected by a multitude of factors; therefore, dietary impact on risk may result from the effect of interactions among foods and food constituents that are difficult to identify from epidemiologic observations. For example, a case-control study in Shanghai found the relative risk of breast cancer in women who excreted large amounts of both phenols and isoflavonoids was only 0.14 (95% CI, 0.02 to 0.88), whereas the excretion of phenols was by itself not protective.[229] Finally, genetic differences, such as those that result in differences in the metabolism of carcinogens, may determine whether a given individual is sensitive to dietary influences.

Cancer Rates in Vegetarians

Vegetarians have an overall lower cancer rate than the general population. What is not clear is to what extent, if any, diet is responsible for this difference. Vegetarians are generally more health conscious, smoke less, drink less alcohol, are often more highly educated, and are leaner than the general population. Consequently, differences in cancer rates between vegetarians and nonvegetarians are probably the result of a multitude of factors. After controlling for nondietary cancer risk factors, differences in cancer rates between vegetarians and nonvegetarians are not striking.

In a collaborative analysis of five prospective studies involving vegetarians that included over 76,172 men and women (27,808 vegetarians), Key et al found that after adjustment for age, sex, and smoking status, vegetarian diet was not associated with a reduced mortality risk for stomach, colorectal, lung, breast, or prostate cancer.[35] Similarly, no protective effect of vegetarian diet was found when comparing subjects who had been vegetarians for at least 5 years to more recent vegetarians or to nonvegetarians.[35] It should be noted, however, that the reference group in this analysis included subjects who ate meat as infrequently as one time per week and, in many cases, had cancer mortality rates that were lower than the general population.

Much of our understanding about vegetarian cancer rates comes from studies involving SDAs. Approximately half of the SDAs in the cancer age range (>40 years) are adult converts to the church, with the remaining half either being born into an Adventist home or joining the church before 20 years of age.[230] Initial reports that SDAs (including both vegetarians and nonvegetarians) had lower overall cancer mortality rates, and specifically lower rates for cancers of the lung, esophagus, bladder, stomach, colon-rectum, pancreas, breast, cervix, and ovary, as well as leukemia, were not adjusted for socioeconomic status (SES).[34] This is important because the church members tend to be of above-average SES, and people of higher SES in the United States are generally at a lower cancer risk.

Based on information collected from participants in the AHS-2, about 36% of SDA church members are vegetarians, and approximately 88% of these are lacto-ovo vegetarians.[231] Historically, however, a higher percentage of vegetarian Adventists have followed a lacto-ovo vegetarian diet, and, consequently, there is relatively little information about the cancer rates of vegans from the first AHS.

In an analysis of the AHS, after adjustment for age, sex, and smoking status, nonvegetarian SDAs had a 54% increased risk for prostate cancer and an 88% increased risk for colorectal cancer in comparison to vegetarians, but incidence rates were similar for lung, breast, uterine, and stomach cancer.[37] The lower colon cancer incidence is consistent with the lower rate of colon cell proliferation in vegetarians,[232] and the prostate cancer data are consistent with results from a study showing that mean serum insulin-like growth factor (IGF)-1 levels were 9% lower in 233 vegan men in comparison to 226 meat eaters and 237 vegetarians ($p = 0.002$).[233] Because of its proliferative effects, higher serum levels of IGF-1 are thought to be involved in the etiology of several cancers.[234–236]

Lower risk of prostate cancer in the AHS-1 was associated with the consumption of dried fruit and possibly tomato and fish.[237] The intake of both red and white meat was independently associated with the higher incidence of colon cancer among nonvegetarians. One of the more intriguing observations from the AHS was that legume consumption was associated with a marked reduction in the incidence of colon cancer ($\geq$3 times/week vs $<$1 time per week; RR, 0.33; 95% CI, 0.13 to 0.83) but only among those who ate red meat. And the positive association between colon cancer and red meat was seen only in those who consumed legumes infrequently. In addition, the consumption of legumes, dried fruits, and meat analogs were each associated with a lower risk of pancreatic cancer, and fruit consumption, after adjustment for smoking, was associated with a lower risk of lung cancer.

In contrast, no significant difference in incidence in colorectal cancer was found among vegetarians in the Oxford Vegetarian Study. And in the EPIC-Oxford, a surprising finding was a higher risk for colorectal cancer among vegetarians, although rates for all cancers combined were lower.[238] In a pooled analysis of data from the EPIC-Oxford study and the Oxford Vegetarian Study, the incidence of all cancers combined was lower among both fish eaters and vegetarians compared to omnivores.[239]

Finally, in a cohort of 37,643 British women in EPIC-Oxford, there was no evidence of an association between vegetarian diet and risk for breast cancer.[240] In contrast, in the UK Women's Cohort Study, women who did not eat any meat had a lower risk for breast cancer,[241] and both red meat and iron intake were positively associated with risk for invasive postmenopausal breast cancer in a prospective study of 52,158 women.[242]

Factors in Vegetarian Diets That May Affect Cancer Risk

Despite the rather modest differences between vegetarians and nonvegetarians in regard to cancer mortality, and even incidence, there are a variety of ways in which vegetarian diet, at least when consumed over the course of a lifetime, may be protective.

Several studies have reported that vegetarians have lower serum or urinary estrogen levels, perhaps because dietary fat and fiber intakes are associated with increases and decreases, respectively,

in estrogen levels. Higher lifetime exposure to estrogen is thought to increase breast cancer risk, and differences in lifelong exposure to estrogen have been suggested as the partial or complete explanation for the variation in breast cancer mortality among countries.[243–252]

Pike et al has estimated that later menses and earlier menopause may explain as much as 80% of the difference in breast cancer mortality rates between Japan and the United States.[243] Vegetarians may begin menstruation at a later age than omnivores.[253,254] In addition to lower estrogen levels, breast cancer risk may be affected by the way in which estrogen is metabolized. Evidence suggests that foods such as cruciferous vegetables and soy alter estrogen metabolism in a way that reduces breast cancer risk.[221,255–258]

In addition to their higher fiber intake, the environment of the colon in vegetarians differs significantly from nonvegetarians in ways that could favorably affect colon cancer risk. For example, vegetarians have a lower concentration of potentially carcinogenic bile acids[259–263] and possibly also lower amounts of bacteria that convert the primary bile acids into the more carcinogenic secondary bile acids.[264–268] Furthemore, colon pH is lower, which would tend to decrease the activity of enzymes responsible for converting primary bile acids into secondary bile acids.[269,270] Vegetarians also have larger and heavier feces and experience more frequent elimination,[263,271,272] which may limit contact between potential carcinogens and the lining of the colon.[273] Fecal weight is related to fiber intake and is inversely related to the incidence of colon cancer among countries[274] (Figure 2-5).

Vegetarians also have lower levels of enzymes that hydrolyze conjugated xenobiotics, thereby enhancing the elimination of potential colon carcinogens.[244,259] Finally, most studies indicate that vegetarians have lower levels of fecal mutagens.[275–278]

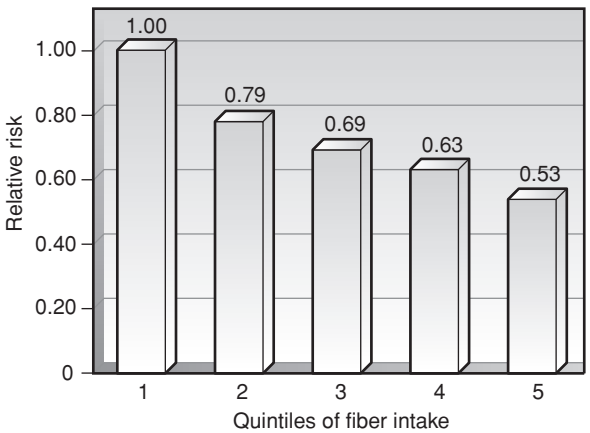

Figure 2-5 Relationship between fiber intake and risk of colon and rectal cancer. Data are based on 13 studies involving 5225 cases and 10,349 controls. The inverse trend between fiber intake and colorectal cancer risk was statistically significant ($P < 0.001$). If causality is assumed, these data suggest that increasing fiber intake by approximately 13 g/d could reduce risk of colorectal cancer by approximately 31% in the United States. Dietary fiber intake in the highest quintile was approximately 31 g/d. *Source*: Data from Smith-Warner et al.[225]

Diet may contribute to the large differences in prostate cancer rates among countries. In Japan and other Asian countries, the incidence of histologic prostate cancer is similar to that in the United States, but the incidence of clinical prostate cancer is much lower, suggesting that some factor common to the Japanese culture delays the onset and/or slows the growth of prostate tumors.[279] Interestingly, the size of the prostate gland does not increase with age among Japanese men as it does in white men.[280]

Some studies have found that high-fiber intake decreases, whereas high-fat intake increases, risk of prostate cancer.[279,281–283] Animal fat in particular may raise risk.[284] There is also some evidence, although the data are inconsistent, that vegetarian diet may affect hormone levels in a way that lowers prostate cancer risk.[285–288] In animals, low-fat diets have been shown to slow the growth of tumors established from human prostatic adenocarcinoma cells.[289] Soybean isoflavones have been shown to inhibit the growth of chemically induced tumors and inhibit the metastasis of existing tumors.[290,291] (See Chapter 9 for a discussion of soy and prostate cancer.)

There has been much enthusiasm for the protective effects of lycopene,[292] selenium,[293] and vitamin E[294] against prostate cancer. However, the results of the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which included 35,533 men, showed neither vitamin E nor selenium alone or in combination helped to prevent prostate cancer in healthy men.[295] In the Physicians Health Study, neither vitamin E nor vitamin C was associated with reduced risk.[296] Finally, high serum vitamin D levels may be protective against prostate cancer, which, according to one school of thought, accounts for the positive association between dairy consumption and prostate cancer risk, as discussed later.[297]

Animal Products and Cancer

International studies show that meat- and dairy-based diets are associated with an increased incidence of breast, colon, prostate, renal, and endometrial cancer.[298] Whether animal products specifically increase cancer risk or whether animal-based diets are associated with a higher risk of certain cancers because they are lower in protective plant components, such as fiber, phytochemicals, and antioxidants, is unknown.

An expert panel commissioned by the WCRF/AICR authored one of the most comprehensive reviews on the subject of diet and cancer, categorizing evidence of risk into four different categories: convincing, probable, possible, and insufficient. The evidence that meat increased colorectal cancer risk was rated as convincing in the 2007 report. Red meat intake was also associated with increased risk for colorectal cancer in a subsequently published large prospective study.[299] In a qualitative overview of the epidemiologic evidence, Huxley et al found high meat intake was associated with a 20% higher risk of colorectal cancer.[300] In the EPIC study, red and processed meat intake was also positively associated with risk for some types of stomach cancer[301] and possibly bladder cancer[302] but not ovarian[303] or breast cancer.[304]

O'Keefe et al found that the low rate of colon cancer mortality among South African blacks was likely a result of their low animal product intake, not their high fiber intake, as had been proposed by Burkitt et al 40 years ago.[305] Their research showed that colon cell proliferation, an indicator of risk, was lower among blacks than white South Africans, which is consistent with the lower colon cancer rates among blacks, but the intake of fiber by these two groups was similar,

whereas the intake of meat was much higher among whites. In support of this finding are four case-control studies, three in Asian countries, which found red meat consumption to be associated with increased colon cancer risk.[306–309] However, other analyses have concluded that meat does not directly cause colorectal cancer, or any other form of cancer, but rather is only coincidentally related to cancer risk.[310–311] Most importantly in this regard, in a 2009 meta-analysis that included six prospective studies, no support for an independent association between either animal fat intake or animal protein intake and colorectal cancer was found.[312]

The relationship between meat intake and breast cancer risk is also unclear. Although a case-control study in southern France found that breast cancer risk increased by 50–60% for each additional 100 g of meat consumed daily,[313] several other studies have not confirmed this type of relationship[304, 314–318] One theory is that meat intake increases risk primarily if consumed during adolescence.[319] Red meat intake has also been linked to prostate[283] and lung[320]cancer.

Although the data on the relationship between animal food intake and cancer are conflicting, there are a number of proposed explanations for the hypothesized carcinogenic effects of meat. For example, heterocyclic amines (HCAs), which are potent mutagens, are formed when meat is cooked at high temperatures, especially when it has been grilled.[321] In experimental models, HCAs have been shown to increase risk for a wide array of cancers, including cancer of the liver, lung, breast, and small and large intestines.[322] Higher temperatures increase HCA formation, whereas microwaving foods produces only small amounts of mutagens. HCAs are also present in pan scrapings and fat drippings.[322] As noted previously, some evidence suggests the association between meat and cancer is particularly pronounced in people who rapidly metabolize certain putative carcinogens.[323] High levels of meat also increase fecal ammonia and N-nitroso compound concentration, which could increase colon cancer risk.[324]

Although quite speculative, the cholesterol in meat, by increasing the level of cholesterol in the large intestinal lumen that is then subject to extensive oxidation, could lead to mutagenic metabolites.[325] And finally, dietary heme may lead to the formation of highly cytotoxic factors in the colonic lumen, which may damage the colonic mucosa resulting in hyperproliferation and an increased colon cancer risk.[326]

One of the more intriguing observations about the relationship between animal product intake and cancer risk is that high dairy consumption increases risk of prostate cancer. A comparison of food intake in 42 countries found milk consumption to be the dietary factor most closely associated with prostate cancer risk.[327] High calcium and dairy intake were found to increase risk for prostate cancer in a Swedish case-control study[328] and in the Health Professional's Follow-Up Study, a prospective study of 20,885 men. In the latter study, calcium from both foods and supplements were linked to increased risk.[329] Among 142,251 men in the EPIC study, a 35 g/d increase in dairy protein was associated with a 32% increased risk in prostate cancer. Calcium from dairy products was also associated with risk but not calcium from other foods.[330]

High intakes of calcium and phosphorus, largely from dairy products, are believed to lower circulating $1,25(OH)_2D$ levels, which may increase prostate cancer risk.[297] In addition, sulfur-containing amino acids from animal products because they lower blood pH, which suppresses 1,25(OH)2D production, will also increase prostate cancer risk. However, the evidence is too

preliminary to draw any firm conclusions about this hypothesis. In contrast to findings regarding calcium and prostate cancer risk, calcium may be protective against colorectal cancer.[331]

DIABETES

The prevalence of diabetes is reaching epidemic proportions throughout the world as rates increase in both developed and developing countries. Type 2 diabetes is now common even among children. Differences in disease rates among countries and regions within countries, in combination with migration data, indicate that lifestyle plays a critical role in the etiology of this disease.[332,333] Obesity is clearly the single most important risk factor for type 2 diabetes,[334] and weight loss in overweight diabetics is the most effective treatment. International comparisons generally show that the prevalence of diabetes correlates positively with serum cholesterol levels and with intake of fat, animal fat, protein, animal protein, and sugar and correlates negatively with intakes of carbohydrates and vegetable fat.[335] A Western dietary pattern high in processed meats has been associated with greater risk for diabetes.[336]

There is some evidence that vegetarians are less likely to develop diabetes. Rates of diabetes among SDAs are less than half (47% for men, 45% for women) those of the general population. Within the Adventist population, vegetarians have lower rates of diabetes than nonvegetarians. In the AHS, the prevalence of diagnosed diabetes at the outset, after adjusting for age and weight, was 1.9 and 1.4 times higher in nonvegetarian men and women, respectively, than in vegetarian men and women.[337] During the 21-year follow-up of individuals without a history of diabetes, the age-adjusted risk of diabetes appearing on a death certificate for nonvegetarians compared with vegetarians was 2.2 fold and 1.4 fold for men and women, respectively. After adjusting for weight, however, risk was still 80% higher in nonvegetarian men but was no longer elevated in women. In a later analysis of the AHS, the age-adjusted risk of developing diabetes for vegetarian, semi-vegetarian, and nonvegetarian men was 1.00, 1.35 and 1.97, and for women was 1.00, 1.08, and 1.93, respectively.[60] And analyses based on cross-sectional data obtained at baseline from participants in the AHS-2 suggests that risk for diabetes is lower by nearly half for vegetarians compared to nonvegetarians after adjusting for lifestyle factors and BMI.[338] In this study, even occasional meat or fish consumption increased risk.

In Adventist men, meat consumption was directly associated with an increased risk of diabetes. Relative risks for men consuming meat 1 to 2 days per week, 3 to 5 days per week, and $\geq$6 days per week were 1.3, 1.5, and 2.4, respectively, compared with vegetarian men.[337] Among women, only those consuming meat six times or more per week were at an increased risk relative to vegetarian women. In this study, nonvegetarian men and women were 1.9 and 1.6 times as likely to be overweight compared with vegetarian men and women. However, in a recent prospective cohort study of 8401 subjects, from the Adventist Mortality Study and the Adventist Health Study, weekly consumers of all meats were 29% more likely to develop diabetes. Long-term adherence (over a 17-year interval) to a diet that included at least weekly meat intake was associated with a 74% increased risk for diabetes relative to long-term adherence to a vegetarian diet.[339] Red meat intake was also associated with increased risk of diabetes in the Women's Health Study.[340]

Hua et al found that in a comparison of 30 lacto-ovo vegetarians and 30 meat eaters, the vegetarians were more insulin sensitive and also had lower body iron stores. Interestingly, when iron stores of the meat eaters were reduced by phlebotomy to levels comparable to those of the vegetarians, insulin sensitivity improved.[341] And in agreement, in a study of 98 healthy Taiwanese women, lacto-ovo vegetarians had significantly lower levels of fasting insulin and plasma glucose and also lower insulin resistance.[342] Insulin sensitivity was also better in a group of Chinese vegetarians compared to omnivores and correlated with years on a vegetarian diet.[343]

One reason for the lower diabetes risk among vegetarians may be that vegetarian, particularly vegan, diets have been found to have a lower glycemic index,[344] and they include foods that may reduce risk of diabetes including nuts,[345] legumes,[346] and fruits and vegetables.[347]

The metabolic consequences of vegetarian diets as they relate to diabetes and insulin sensitivity are discussed in Chapter 16. Clearly, though, the protective effects of vegetarian diets against heart disease offer an important advantage to diabetics given that their risk of CHD is increased more than threefold compared to nondiabetics.[348] Intervention studies have shown benefits of low-fat vegan diets for reducing both LDL-C levels and glycosylated hemoglobin.[61]

OBESITY

Obesity is becoming the number-one health problem in the United States as its prevalence continues to increase. Currently, nearly two thirds of Americans are overweight. The prevalence of obesity (generally defined as $\geq$20% overweight) reaches 50% in some populations, particularly Native American, African American, and Hispanic women.[349,350] Obesity is much more common in American women below the poverty line, whereas in men it is more common above the poverty line.

Research on the BMI and body fat content of vegetarians compared with nonvegetarians is summarized in Appendixes D and E. Collectively, these studies indicate that vegetarians are either similar to nonvegetarians or have lower BMIs and/or less body fat. Differences between vegetarians and nonvegetarians were likely minimized in many studies, however, because of the selection criteria for study subjects (i.e., obese people were often ineligible). In the EPIC-Oxford Study, Spencer et al found that on average, vegetarians have a BMI about 1 kg/m^2 lower than that of nonvegetarians, which leads to obesity rates that are only about half those of vegetarians, with vegans having lower rates than other vegetarians.[351] During 5 years of follow-up, small differences in weight gain were observed among meat eaters, fish eaters, vegetarians, and vegans, and the lowest weight was seen among those who reduced their animal food intake during the follow-up period.[352] In the AHS, BMI increased as frequency of meat consumption increased.[37] And among Adventists in Barbados, those who had been vegetarian for $<$5 years had BMIs similar to nonvegetarians; those who had been vegetarian for at least 5 years were 70% less likely to be obese compared to nonvegetarians.[353] The lower BMI of vegans in comparison to lacto-ovo vegetarians in an analysis by Spencer et al is consistent with the findings from several smaller studies.[351,354,355]

Differences in levels of physical activity do not appear to contribute to the lower BMI/body fat of vegetarians because several studies indicated little if any difference between the two groups in this regard.[42,356–359] In the Oxford Vegetarian study, the lower BMI of non–meat eaters was associated in part, with a higher intake of fiber, and a lower intake of animal fat, and in men only, a lower intake of alcohol, but this explained only a third of the difference in BMI.

The effect of calcium and dairy products on weight management is an area of ongoing research. One pilot study showed that fortified soymilk was as effective as skim milk in promoting weight loss.[360] In fact, a comprehensive analysis of the data published in 2008 concluded that soyfoods are as effective as other protein sources for promoting weight loss and found a suggestive body of evidence that soyfoods may confer additional benefits.[361]

Interestingly, vegetarians may have a higher metabolic rate than nonvegetarians. In a study of lacto-ovo vegetarians and vegans in their mid-20s, resting metabolic rate (RMR) was 11% higher in vegetarians than in nonvegetarians. This was at least partly due to a higher level of plasma norepinephrine, which could result from the higher carbohydrate and lower fat intake of vegetarians.[362] Previous studies found a trend toward a higher RMR in male [363] but not female[364] vegetarians. Also, based on differences in urinary amino acid excretion, Hubbard et al speculated that vegans had higher amino acid metabolic activity.[365] Vegetarian diet per se, however, may be no more effective in producing weight loss than other dietary patterns that emphasize low fat and high carbohydrate intake.[366,367]

KIDNEY DISEASE

In 1982, Brenner et al first hypothesized that glomerular capillary hypertension, which is associated with increased glomerular filtration rates, results from an unrestricted intake of protein-rich foods and can lead to the progressive decrease of renal function seen in aging.[368] The relationship between protein intake and renal function is not without uncertainty, [369] but one school of thought is that high dietary protein may exacerbate existing kidney disease and increase the risk for developing renal disease.[370,371] Because vegetarian protein intake is adequate but lower than omnivore intake, vegetarian diets may have a role in the prevention and/or management of kidney disease. In fact, the glomerular filtration rate (GFR) of healthy vegetarians is lower than that of healthy nonvegetarians (based on creatinine clearance), and vegans have an even lower GFR than lacto-ovo vegetarians.[372]

Dietary protein increases the GFR in healthy individuals.[373] Furthermore, in healthy people without kidney disease, factors that increase the GFR may negatively affect kidney health, especially in those who are susceptible to developing kidney disease and in the elderly because kidney function declines with age. Support for the Brenner et al hypothesis comes from a study of 2500 older subjects who reported previous kidney problems. Consuming an additional 15 g of protein was associated with a 25% increase in overall mortality during the 14-year follow-up period.[374]

Findings indicate that the type of protein consumed may also affect kidney function. For example, GFR was shown to be 16% higher in healthy subjects after eating a meal containing animal protein in comparison with a meal containing soy protein (Figure 2-6).[375] Similarly, challenging the kidneys of healthy subjects with a high dose of meat protein adversely affected a variety of kidney function parameters in comparison with a challenge with soy protein.[376] Kontessis et al found that in normotensive, nonproteinuric subjects with type 1 diabetes, consuming a diet in which all of the protein was derived from plant foods resulted in more favorable effects on renal function than consuming a diet in which 70% of protein was derived from animal products.[377] In the Nurse's Health Study, animal protein but not overall protein intake was associated with continued loss of renal function in women who had some degree of renal impairment at

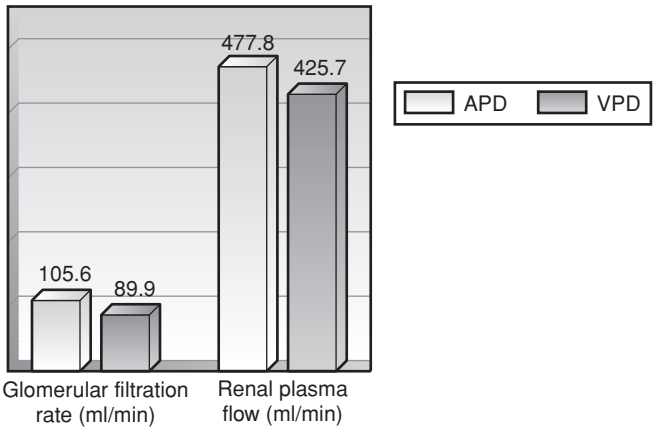

Figure 2-6 Effects of vegetarian diet on kidney function in diabetic subjects. Kidney function was studied in nine normotensive, nonproteinuric individuals with non-insulin-dependent diabetes mellitus fed in random order for 4 weeks either an animal protein diet (APD; protein intake 1.1 g/kg per day) or a vegetable protein diet (VPD; 0.95 g/kg per day) with similar caloric densities. Differences in glomerular filtration rate and renal plasma flow between the two dietary periods were notably significant ($P < 0.05$, Wilcoxon's signed rank test). *Source*: Data from Linos et al.[319]

baseline.[371] And in one study, removing red meat from the diet while keeping protein intake constant, reduced urinary protein losses in patients with diabetes.[378]

Among healthy Thai women, urinary protein levels were significantly lower in vegans compared to nonvegetarians.[379] The consumption of a vegetarian diet that included soy protein was shown to reduce urinary protein excretion in nephrotic patients.[380] The protective effect of protein restriction is most apparent in diabetic nephropathy[381] and advanced renal disease.[382]

However, not all studies have found that plant proteins have favorable effects on renal function. Soroka et al fed a low-protein, soy-based vegetarian diet or an animal-based diet to 15 patients with chronic renal failure and found that after 6 months, both diets were equally effective in retarding the progression of renal failure.[383] They suggested that these findings may have differed from much of the literature because subjects in their study had interstitial types of renal disease, rather than glomerular diseases associated with marked proteinuria. However, they did find that compliance with the vegetarian diet was better than the animal-based diet, and that phosphorous intake and urinary phosphate excretion were lower on the vegetarian diet, which could be an advantage for predialysis and dialysis patients.[384]

Finally, because the pathology of kidney disease is now thought to be similar to that of atherosclerosis, reducing high serum cholesterol levels and inhibiting cholesterol oxidation are thought to be important for reducing risk of developing kidney disease and for preventing the deterioration of kidney function in patients with existing kidney disease.[385,386] Consequently, vegetarian diets may offer additional protection against kidney disease because cholesterol levels are lower in vegetarians and because their intake of antioxidants is higher than that of omnivores, as discussed

previously. The combination of reduced intakes of saturated fat, protein, and animal protein and higher intake of antioxidants suggests that vegetarian diets may be useful in both prevention and treatment of kidney disease. Because soy protein may favorably affect renal function and lower serum cholesterol, substituting soy protein for animal protein may be particularly helpful for those with renal problems.[387]

RENAL STONES

Renal stones affect 10–15% of Americans and are more common in men than women.[388,389] Renal stones may be 10 times more common today than they were at the beginning of the 20th century[390] and are a public health problem particularly in affluent countries.[391] About 80% of all renal stones are composed of calcium oxalate, sometimes with a nucleus of calcium phosphate. Oxalate is present in foods and is also synthesized endogenously. Contrary to a long-held belief, consuming diets high in calcium does not appear to increase risk for renal stones; rather, calcium seems to reduce risk (although calcium supplements may increase risk).[392,393] The reason may be that calcium binds oxalates in foods and in the intestines, making less oxalate available for renal stone formation.

As discussed in Chapter 3, protein in general, and animal protein in particular, may enhance urinary calcium excretion.[394] This may explain why people who have recurrent bouts of kidney stones tend to eat diets high in animal protein.[395–398] One large prospective study involving 45,000 men found a 30% increased risk of renal stone formation associated with above-average protein intakes.[392] In support of this observation is the finding that vegetarians appear to have a lower incidence of renal stone formation. A survey of approximately 2500 British vegetarians, 73% of whom were lacto-ovo vegetarians, found that the prevalence of urinary stone formation was roughly half that of the general population.[399] Brockis et al found that increased intake of animal protein was associated with an increase in the urinary output of compounds that raised risk of renal stone formation by 250%.[395] Based on such evidence, Robertson et al suggested a more vegetarian diet as a means of reducing the risk of stone recurrence.[397] On the basis of a review of the data, Zuckerman et al recently recommended a diet high in fluid and citrus fruits, with normal calcium, and restricted sodium, oxalates, and animal protein for the prevention of kidney stones.[400] Meat protein in particular appears to cause an imbalance between promoters and inhibitors of urinary crystallization by at least five mechanisms.[401] Some research suggests that patients with chronic renal stones are more likely to consume high-sodium diets that tend to be moderate or low in potassium.[402]

Although most kidney stones are comprised primarily of calcium oxalate, they may also be formed of uric acid. Uric acid is derived primarily from the metabolism of purines, which are highly concentrated in meat, although some plant foods (e.g., lentils) are also high. Breslau et al found that when subjects switched from a vegetarian diet, in which most of the protein came from soy and some cheese, to a mixed diet containing both animal and plant protein, to one in which protein came predominantly from animal sources, dietary purine intake increased from 1 to 2 to 72 mg/d, respectively.[403] Others have found that a diet rich in animal protein causes a doubling of urinary excretion of urate.[404–406] Citrate, an organic acid that is abundant in plant foods, interferes with kidney stone formation.[407] Urinary pH also influences stone formation.

Animal proteins tend to decrease urinary pH, and a low pH is thought to increase the risk of forming both types of kidney stones.[408] For these reasons, vegetarian diets may offer additional protection against renal stone formation.

Inadequate fluid intake raises risk for kidney stones, which may explain a higher incidence in warm climates. The American Urological Association projects that global warming will lead to increased prevalence of kidney stones.

GALLSTONES

Gallstones, one of the main components of which is cholesterol, are the major cause of gallbladder disease in the United States, affecting approximately 10% of the population. They are as much as three times more common in women as in men. In Japan, the incidence of gallstones increased by a factor of 5 between 1950 and 1975.[409] During this time the intake of animal protein and fat increased by 129% and 190%, respectively. In contrast, rural Africans, who consume a largely vegan diet, rarely if ever develop gallstones.[410] Similarly, vegetarians are much less likely to develop gallstones than meat eaters.

In a study of >800 women between the ages of 40 and 69 years, Pixley et al found that only 12% of the vegetarians but 25% of the nonvegetarians had gallstones.[411] Many factors have long been thought to be risk factors for gallstones, but of these only obesity, gender, and aging have been confirmed.[412] Even after controlling for these factors, however, vegetarians were still only half as likely to develop gallstones as meat eaters.[411]

Why vegetarians have a reduced risk is uncertain. Some studies have found that higher intakes of calories, saturated fat, and simple sugars increase risk, whereas moderate alcohol consumption and fiber decrease risk.[413] Legume intake[414] and the intake of lecithin-containing foods may also help prevent gallstones.[415] An anthropometric advantage for vegetarians may be their leanness because obesity increases risk for gallstones. Although speculative, vegetable protein, in particular soy protein, may also have some advantages for reducing the risk of developing gallstones.[416,417]

Finally, there is evidence that sedentary lifestyle, a diet rich in animal fats and low in fiber,[418] folate, calcium, vitamin C, and magnesium has also been associated with increased risk.[419,420]

DIVERTICULAR DISEASE

Diverticular disease has been referred to as a deficiency disease of Western civilization, referring to the lack of fiber in Western diets.[421] It is characterized by pouching and inflammation of the wall of the bowel. This defect is common in Western industrialized nations and is estimated to occur in 60% of people at least 60 years of age in the United States. Symptomatic diverticular disease results in 200,000 hospitalizations in this country annually.[422] As recently as 1916, however, the disease was not prevalent enough to merit a mention in medical textbooks. Research indicates that diverticulitis is less common in vegetarians.[423]

In a study conducted by Gear et al, both male and female vegetarians ≥45 to 59 years of age were only 50% as likely to have diverticulitis as nonvegetarians.[423] The effects of vegetarian diets on diverticular disease are probably due to their increased fiber content, especially the insoluble cereal fibers, such as wheat bran. Bran has been shown to be useful in the treatment of diverticu-

lar disease,[424] although research also suggests that fiber from fruits and vegetables is helpful.[425] In the study by Gear et al, vegetarians consumed 41.5 g of fiber per day, whereas meat eaters consumed only 21.4 g/d. Fiber increases fecal bulk and presumably decreases colon pressure, so that the products of digestion are more easily propelled through the colon.[426] Stool weights of vegetarians were shown to be two to three times those of omnivores and of individuals with diverticular disease in one study.[427]

Other factors common to Western diets may also play a role in promoting diverticulitis. In a prospective study involving >40,000 U.S. health professionals, high-fat diets increased risk of diverticulitis independent of fiber intake.[428] Men on a high-fat, low-fiber diet were more than twice as likely to develop the disease. Findings also suggest that the insoluble component of fiber, especially cellulose, is significantly associated with a decreased risk of diverticular disease.[428] Even more striking, men on a high-red meat, low-fiber diet, were more than three times as likely to develop diverticulitis, suggesting that meat may increase risk.[425] A Taiwanese case-control study that included 192 subjects found an association between past meat consumption and diverticulosis.[429] These findings support a previous observation that red meat intake may promote the growth of bacteria that produce a toxic metabolite or a spasmogen that weakens the wall of the colon and favors the formation of diverticula.[430] In an analysis of U.S. health professionals, vigorous activity, such as running and jogging, was also very protective; in fact, sedentary men who consumed low-fiber diets were 2.5 times more likely to develop diverticulitis than men who ran or jogged for exercise and consumed high-fiber diets.[431] Contrary to popular belief, the evidence does not support restriction of seeds and nuts for those with diverticular disease.[432,433]

OTHER CONDITIONS

Vegetarians may be less likely to suffer from a number of other conditions, although the evidence is not nearly as strong as for those diseases previously discussed.

Rheumatoid Arthritis (RA)

Arthritis is a general term for inflammation of the joints. Rheumatoid arthritis (RA) is the most common form of arthritis, affecting 0.3–1% of the general population. Approximately 150 studies have found dietary influences on RA, but poor methodology was used in most of these studies.[434] Several studies, primarily from one group of researchers in Finland, have suggested some relief from a vegan diet that includes substantial amounts of raw foods.[435–443] In a comprehensive review on this subject, Grant found that fat from meat, based on food disappearance data, was found to have the highest association with the incidence of RA among countries, and concluded that rather than fat, the nitrite contributed by meat intake might be the responsible agent.[444]

Some evidence indicates that RA is less common among those who adhere to a Mediterranean-type diet[445] and that the diet could be beneficial in treatment of symptoms.[446] However, in a review of RCTs, Hagen et al concluded that effects of dietary manipulation, including vegetarian, vegan, Mediterranean, and elimination diets on RA remain uncertain due to study weaknesses.[447]

Gout

The formation of crystals in the joints results in an inflammatory disease known as gout. These crystals contain uric acid, a breakdown product of purines. Only about 15% of the urate formed each day comes from dietary sources. Most comes from the normal turnover of nucleic acids. Alcohol appears to be the main dietary component associated with gout, but a diet restricted in purines can also be of some help. High-purine foods include fish, liver, and kidneys. All meats are moderately high in purines, as are some legumes. A diet high in meat and seafood has been associated with greater risk for gout.[448] Weight loss, and possibly a diet that increases insulin sensitivity, may have some advantages for the management of gout.[449] Vitamin C intake may also reduce risk for gout.[450]

Dementia and Alzheimer's Disease

Dementia is an increasing economic and public health problem. In 1997, 2.32 million people had Alzheimer's disease (AD), 68% of whom were women. More striking, the prevalence of AD in the United States is expected to triple by 2050.[451] Rates of dementia vary throughout the world, even when adjusted for age, but comparisons are difficult because of differences in diagnostic criteria.[452] Nevertheless, rates appear to be lower in Asia, and, the most common type of dementia among white populations is AD, whereas in Asia, it is vascular dementia.[452] In both cases, though, the incidence of dementia rises exponentially with age. The annual incidence rate at 70 to 74 years of age is only 0.506, but by age 85 to 90 years, it is 3.858.[453] Because of the age-related nature of this disease, interventions that can delay the onset of AD by as little as 5 years could decrease prevalence by 1 million cases after 10 years.[454]

Preliminary data suggest that diet may impact AD and dementia. One report indicated that vegetarian diets may offer some benefits in regard to cognitive function because among SDAs, those who ate meat were found to be more than twice as likely to develop dementia.[455] If they had been eating meat for many years, they were more than three times as likely to show symptoms. One theory is that free radicals might be involved in the onset of dementia.[456] There is observational support for the benefits of diets high in antioxidants and that antioxidant supplements may retard age-related dementia,[457–459] although not all studies are supportive.[460] More specifically, the intake of flavonoids was found to be associated with a reduced risk of developing dementia.[461] Interestingly, serum vitamin C levels are lower in AD patients despite an adequate intake.[462] Because vegetarian diets are higher in the antioxidants that protect against free radical damage, this might also contribute to a reduced risk of senile dementia among vegetarians.

There are also data indicating that prior stroke and hypertension are related to dementia, so the lower blood pressure of vegetarians should be an advantage in this regard.[463–465] Furthermore, prevalence of probable AD was reduced by 60–73% in patients taking statins, suggesting cholesterol reduction may be an effective means to prevent AD and dementia.[466,467]

Estrogen therapy was initially postulated to reduce risk of AD and age-related cognitive impairment, but more recent data have shown equivocal results in regard to benefits. There may be a particular window of time during which estrogen therapy is protective in postmenopausal

women. Because of the interest in estrogen, the relationship between phytoestrogens and cognition has received attention (see Chapter 9 for discussion of this issue).[468–471]

Finally, there is considerable interest in the relationship among the intake of folate and vitamin B_{12}, homocysteine levels, and dementia.[472–476] The possibly protective effects of higher serum folate levels might work to the advantage of vegetarians, but as discussed previously, vegetarian homocysteine levels are similar to or higher than levels in omnivores, a likely result of the poorer vitamin B_{12} status of vegetarians.

Constipation and Hemorrhoids

A specific definition of constipation is likely to vary from person to person, but technically constipation is characterized by hard stools and elimination fewer than three times per week. Constipation affects approximately 5 million Americans, but surveys show that up to 10% of children suffer from chronic constipation.[477] The consumption of adequate liquids and fiber is the best approach to avoiding constipation. Hippocrates observed that certain food items of plant origin (fruit, vegetables, bran) resulted in soft stools.[478] Insoluble fiber, such as that found in wheat bran, is especially helpful.[479] Lack of fiber was recently suggested as a causative factor in chronic idiopathic constipation in children,[480] and fiber was shown to alleviate constipation in a

Exhibit 2-2 Factors Common to Vegetarian Diets that Have Been Associated with Reduced Risk for Chronic Disease

Factor	*May protect against*
Lower saturated fat intake	Heart disease, gallstones
Lower cholesterol intake	Cancer
Lower animal protein intake	Renal disease, renal stones
Higher plant protein intake	Hypertension
Higher fiber intake	Heart disease, colon cancer, diverticular disease, hypertension, gallstones
Higher fruit and vegetable intake	Hypertension, cancer
Higher antioxidant intake	Heart disease, cancer, renal disease
Higher nut intake	Heart disease, diabetes
Lower glycemic load	Hypertension, diabetes
Higher nonheme iron intake	Hypertension
Absence of dairy (vegans)	Prostate cancer
Absence of red meat	Colon cancer, breast cancer, bladder cancer, diabetes
Higher soy intake	Breast cancer, prostate cancer
Higher legume intake	Gallstones

group of children.[481] Constipation may have serious consequences because frequent constipation may be an important risk factor for colon cancer.[482]

Straining due to constipation can result in hemorrhoids, which are clusters of enlarged veins near the rectum. Because vegetarians consume 50–100% more fiber than meat eaters, they are less likely to suffer from either constipation or hemorrhoids.[483–491]

Conclusion

Vegetarians have lower rates of cancer (particularly colon and lung cancer), heart disease, hypertension, diabetes, gallstones, kidney disease, and colon disease. The extent to which vegetarian diet plays a role in the better health of vegetarians is not easy to determine, but the evidence

Case Study

Harold is a 63-year-old man with a history of elevated blood cholesterol and hypertension. He has a strong family history of heart disease. Since adopting a lacto-ovo vegetarian diet 2 years ago, he has lost 15 pounds and is close to his goal weight, and both his cholesterol and blood pressure have dropped, but not to his goal levels. He works full time as an accountant and buys his lunch most days from a cafeteria or restaurant. He sometimes brings snacks to work or else buys them from a vending machine.

24-hour recall

Breakfast
- 2 oz Kellogg's Corn Flakes
- 1 cup skim milk
- ½ English muffin with 1 tbsp strawberry jam
- 6 ounces orange juice
- Black coffee
- Snack
- Coffee
- Low-fat granola bar

Lunch
- Hummus wrap with chopped tomato and lettuce
- Small tossed salad with oil and vinegar dressing

Snack
- ½ cup unsalted pretzels

Dinner
- 1½ cups black bean chili
- 1 cup zucchini sautéed in olive oil and topped with 1 tbsp low-fat parmesan cheese
- 2 whole wheat dinner rolls with 2 tsp reduced fat margarine
- 12 oz beer

What changes would you suggest to lower Harold's blood pressure further and to reduce his risk for coronary heart disease?

indicates it is an important factor in many instances. Vegetarian diets differ in many ways from omnivore diets. They are lower in fat (particularly saturated fat), protein, and animal protein and are higher in fiber, complex carbohydrates, antioxidants, and phytochemicals. All these factors may contribute to the health-promoting effects of vegetarian diets. Animal product intake per se may also directly increase risk of some chronic diseases. It is clear that vegetarian eating patterns adhere more closely to guidelines for optimal diet and are similar to the diets of populations with reduced chronic disease risk. Exhibit 2-2 summarizes factors common to vegetarian diets that have been associated with reduced risk for chronic disease.

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