Coffee Consumption has been shown to have adverse effects on various biological markers of coronary heart disease (CHD) risk, including serum cholesterol (1), blood pressure (2), insulin resistance (3), and plasma homocysteine (4). In contrast, higher coffee consumption has not been associated with a higher risk of CHD in prospective cohort studies (5–7). What could be the explanation for this “coffee paradox”? First, the acute effects of coffee consumption can be different from the effects of long-term habitual consumption. Second, the physiological effects of coffee can depend on the type of coffee consumed and are not necessarily the same as for caffeine in isolation. Third, coffee consumption may have beneficial effects on other biological pathways implicated in the development of CHD that could compensate for any adverse effects. Fourth, risk markers may not causally affect the development of CHD, or their effects may be too modest for any increase caused by coffee consumption to translate into a substantial increase in disease risk. Research supporting these explanations are discussed, with particular focus on the association between coffee consumption and homocysteine concentrations reported by Ulvik et al. in this issue of Clinical Chemistry (8).

In caffeine-naive individuals, caffeine intake leads to a marked reduction in insulin sensitivity (3) and marked increases in postload glucose concentrations (9), epinephrine concentrations (10), and blood pressure (10). Within a week of initiating caffeine intake, however, an individual experiences an attenuation of coffee’s effects on epinephrine release and blood pressure (10). For blood pressure, only a partial tolerance develops, and a modest increase remains after several weeks (2). Given that caffeine’s stimulation of epinephrine release appears to contribute to insulin resistance (3), it is plausible that the effect of caffeine on glucose metabolism would also attenuate after continued caffeine intake. There is limited evidence that the increase in insulin concentration caused by high caffeine intake remains after 1–4 weeks (11, 12). In contrast, the results of prospective cohort studies suggest that long-term caffeinated coffee consumption is not substantially associated with a risk of hypertension (13) and may lower the risk of type 2 diabetes (14). Thus, partial tolerance to the effects of caffeine can develop, but longer-term trials on the effects of coffee on biological risk factors are needed to bridge the gap in the data between short-term trials and cohort studies.

With regard to the type of coffee, the effect of coffee consumption on serum cholesterol depends on the brewing method. In randomized trials, high consumption of boiled coffee led to a substantial increase in LDL cholesterol, whereas high consumption of paper-filtered coffee had little effect (1). The diterpene cafestol has been identified as the cholesterol-raising component of coffee (15). For paper-filtered coffee, the filter prevents substantial amounts of cafestol from getting into the coffee, whereas cafestol remains in boiled, French press, and Turkish/Greek coffee (15). Coffee is a complex mixture of hundreds of plant compounds that may interact in their physiological effects. Most research on coffee components has focused on caffeine, and it is tempting to directly extrapolate the physiological effects that have been found for caffeine in isolation to those of coffee. However, the effects of coffee on exercise performance (16), epinephrine concentrations (16), blood pressure (2), and hyperglycemia (9) all appear to be weaker than the effects of the same amount of caffeine used in isolation. Recently, the acute effects of caffeine, caffeinated coffee, and decaffeinated coffee on responses to an oral glucose tolerance test were evaluated (9). Compared with placebo, caffeine increased postload glucose concentrations, caffeinated coffee showed a nonsignificant increase, and decaffeinated coffee produced a significant decrease in glucose concentrations. Similarly, trials of caffeinated coffee tended to show weaker effects on blood pressure than trials of caffeine in isolation (2), and the coffee phenol chlorogenic acid may reduce blood pressure (17). In line with these results, the consumption of other caffeine-containing drinks, but not decaffeinated coffee, was associated with a higher risk of developing hypertension (13). These findings suggest that components in coffee other than caffeine have physiological effects that are opposite to those of caffeine. For example, quinides may counteract the adenosine receptor antagonism caused by caffeine (18).

Ulvik et al. report an association between higher coffee consumption and higher plasma homocysteine concentrations in a large population-based cross-
sectional study (8). This finding is consistent with results from previous observational studies (19) and randomized trials (4, 20–22). Both caffeine (20) and chlorogenic acid (21) have been shown to contribute to the homocysteine-raising effect of coffee. Caffeine (1,3,7-trimethylxanthine) has been postulated to possibly inhibit the vitamin B6–dependent breakdown of homocysteine, because it is similar in structure to theophylline (1,3-dimethylxanthine), a known vitamin B6 antagonist (20). Chlorogenic acid may raise homocysteine concentrations because of its involvement in O-methylation reactions: the transfer of a methyl group from S-adenosylmethionine to phenolic compounds produces homocysteine (21). Ulvik et al. report an association between high coffee consumption and lower blood concentrations of folate and vitamin B6, with this association being limited to the population with high concentrations of these vitamins (8). These investigators hypothesize that caffeine may stimulate the urinary excretion of folate and vitamin B6 when circulating concentrations are high. In randomized trials of coffee and chlorogenic acid, reductions in concentrations have been found for vitamin B6 and folate (21). Although this mechanism may contribute to the effect of caffeine on homocysteine concentrations, it is unlikely to fully explain this effect because other trials have found that coffee and caffeine substantially increase homocysteine concentrations in the absence of changes in B vitamin concentrations (4, 20).

Given the observational nature of the study by Ulvik et al., potential sources of bias and confounding effects have to be considered in the interpretation of the results. A cross-sectional study design often complicates the interpretation of the direction of effects; however, people are not generally aware of their B vitamin or homocysteine concentrations. Therefore, the effects of these outcome variables on coffee-consumption habits (“reverse causation”) are unlikely. Confounding variables are more likely to have affected the results, because high coffee consumption tends to be associated with a less health-conscious lifestyle. Indeed, Ulvik et al. report that study participants with high coffee consumption were 3 times as likely to smoke cigarettes (8). It is plausible that high coffee consumption was also associated with a lower intake of folate and vitamin B6 from foods and vitamin supplements, but the authors were not able to adjust for these potential confounders. Therefore, the intriguing hypothesis raised by Ulvik et al. that high caffeine intake reduces B vitamin status requires confirmation in further studies.

Results from recent studies suggest that coffee consumption may also have beneficial effects on biological risk factors for CHD. Coffee has been identified as a major contributor to the in vitro antioxidant capacity of the diet (23). Consumption of coffee acutely increases the concentrations of phenolic compounds in LDL cholesterol particles and platelets, increases ex vivo resistance to LDL oxidation, and reduces platelet aggregation in healthy volunteers (24, 25). Decaffeinated coffee and phenolic coffee components improved insulin sensitivity in animal studies (26, 27), and habitual coffee consumption has been associated with a substantially lower risk of type 2 diabetes in prospective cohort studies (14). Coffee has also been proposed to possibly have beneficial effects on CHD risk through prevention of postprandial hypotension (6) and inflammation reduction (7). Further research on these potential beneficial effects of coffee is required and could lead to the development of types of coffee with improved health effects.

What can we conclude about the paradox of adverse effects of high coffee consumption on various biological risk factors for CHD and an apparent lack of increase in CHD incidence? First, the prospective cohort studies suggesting that coffee consumption is not associated with an increased risk of CHD have been conducted in populations that predominantly consumed paper-filtered coffee (5–7). Effects are likely to be different for consumption of types of coffee high in the cholesterol-raising compound cafestol. Second, the detrimental short-term effects of caffeine intake on blood pressure and insulin sensitivity may be reduced by the development of partial tolerance with long-term use and the counteracting effects of other coffee components. In contrast, the effects of coffee on homocysteine appear to remain after long-term coffee consumption, with both caffeine and chlorogenic acid contributing to this effect. It is unclear, however, whether homocysteine has a causal effect on the development of CHD or is merely an innocent bystander (28). Finally, beneficial effects of coffee on biological pathways involved in the development of CHD may compensate for detrimental effects on other biological risk factors. In sum, currently available knowledge on the effects of paper-filtered coffee on biological CHD risk factors is compatible with the observation that coffee consumption is not associated with a higher risk of CHD in prospective cohort studies. General recommendations to reduce coffee consumption as a means to reduce the risk of CHD do not seem warranted, and public health efforts should prioritize other lifestyle factors, including quitting smoking, increasing physical activity and diet quality, and preventing excess caloric intake.

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References


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