Cardiovascular disease (CVD) remains the leading cause of death in the United States, accounting for $444 billion in healthcare expenditures in 2010.\(^1\)\(^2\) Reducing dietary cholesterol has long been part of the American Heart Association (AHA) and American College of Cardiology (ACC) guidelines on lifestyle management. Current AHA/ACC guidelines state that insufficient evidence exists to determine whether lowering dietary cholesterol intake reduces serum cholesterol, but still recommend limiting intake to less than 300 mg per day.\(^3\) The Therapeutic Lifestyle Changes (TLC) diet promotes less than 200 mg per day\(^4\) and the Dietary Approaches to Stop Hypertension (DASH) diet recommends less than 150 mg per day.\(^5\)

**Relationship Between CVD and Serum Cholesterol**

Although elevated serum low-density lipoprotein cholesterol (LDL-C) is a widely established risk factor for developing CVD, the relationship between cholesterol intake and serum LDL-C remains unclear. The Framingham Study was one of the first to demonstrate that high serum cholesterol increases CVD risk.\(^6\) The study suggested that cholesterol intake be limited, although no association between cholesterol intake (assessed by food frequency questionnaires) and elevated serum cholesterol was detected. Early meta-analyses on the topic suggested that for every 100 mg increase in dietary cholesterol, serum total cholesterol (TC) concentration would increase by 2.2 to 2.5 mg/dL, LDL-C would increase by 1.9 mg/dL, and high-density lipoprotein cholesterol (HDL-C) would increase by 0.4 mg/dL. However, not all subsequent feeding studies have detected a negative effect of dietary cholesterol on serum lipid profiles.\(^7\) Wide variations in response to dietary cholesterol are likely responsible for the observed discrepancies, and researchers have identified so-called “hyper-responders” and “hyporesponders,” which are often used to differentiate individuals.\(^8\)-\(^11\)

The notion that reducing dietary cholesterol promotes reductions in serum cholesterol has been questioned for decades.\(^12\) Researchers have suggested that other dietary and lifestyle factors may play more significant roles in negatively altering lipid profiles and may ultimately pose greater risks to cardiovascular health. To add more controversy and confusion to the debate, a recent study found that the type of statistical approach used to analyze dietary intake data led to differences in the statistical significance of the results.\(^13\) Investigators stated that all diet analyses share the common assumption that the variable in question (usually a specific food constituent) has been measured with a high degree of accuracy, when commonly it is not. Much care and attention should be focused on choosing a statistical method that is unbiased, interpreting the results with caution, and adequately controlling for potentially confounding variables, especially with diet-based epidemiologic studies.\(^13\)

**Past Perceptions of Eggs and CVD**

Reducing dietary cholesterol is one of the unifying characteristics of the DASH, TLC, and AHA/ACC diets. Since one egg yolk typically contains between 185 mg and 265 mg of cholesterol\(^14\), the TLC and DASH diets recommend no more than two and four egg yolks per week, respectively. Older studies have cited significant increases in TC following whole egg consumption; however, these studies failed to assess concentrations in various lipoproteins.\(^15\) Because HDL-C has anti-atherogenic properties, it can be misrepresentative to draw conclusions based solely on TC measurements. In a subpopulation of the Framingham Study, egg consumption was quantified and compared with serum TC measurements. Although researchers found that egg consumption was related to dietary cholesterol intake, no relationships to serum cholesterol, all-cause mortality, coronary heart disease, myocardial infarction, or angina were observed. The researchers concluded that physicians must consider the effect of diet as a whole rather than simply limiting egg consumption.\(^15\) Recent meta-analyses of dose response prospective cohort studies\(^16\) and other prospective studies\(^17\)\(^18\) have failed to link egg consumption with CVD. Others found that HDL-C actually increases with whole egg consumption and moderate carbohydrate restriction in overweight individuals, indicating a potentially protective effect.\(^19\)

To date, no controlled dietary intervention trials have determined a link between egg consumption and CVD in individuals who are at low and at increased risk for CVD. The lack of connection may be explained by two key issues. First, eggs are a rich source of important nutrients including, but not limited to, lutein and zeaxanthin, which are part of the xanthophyll class of antioxidants that may protect against lipid oxidation.\(^20\) Second, increased dietary cholesterol increases circulating LDL-C and HDL-C in hyper-responders following egg consumption, which
results in minimal change in the overall ratio of LDL-C to HDL-C. It is imperative to note that 75% of the population experiences little or no alteration in plasma cholesterol concentration following a high cholesterol challenge. The aforementioned studies have assessed the addition of eggs to free living dietary intake as well as during weight maintenance and moderate carbohydrate (CHO) restriction. It is critical to understand that moderate CHO restriction can independently decrease TG, which may obscure findings in some studies. Studies utilizing such interventions should consider the effect of reduced CHO diets alone when interpreting results.

**Egg Intake in Individuals at Low Risk for CVD**

Limiting egg consumption is often recommended as a means of decreasing CVD risk; however, since the seminal Framingham Study, extensive work has been conducted to confirm the efficacy of this recommendation. Several groups have sought to determine the lipid-altering potential of eggs in high- and low-risk individuals alike. Following is a discussion of egg consumption with and without exercise and its respective lipid modulating effects in individuals at low risk for CVD, along with a discussion of studies that have not utilized weight loss interventions, as this may independently alter blood lipid concentrations.

The cardioprotective effects of resistance and endurance exercise are well-documented, and regular exercise is promoted as a key part of a healthy lifestyle. However, minimal work has been done to assess the concomitant effects of exercise and egg intake on blood lipid concentration. Our group recently demonstrated that the consumption of an egg-based breakfast that added two eggs per day to normal dietary intake for 12 weeks did not alter lipoprotein concentrations in healthy, recreationally trained individuals following a three-times-per-week resistance training program. Furthermore, we determined that egg-based breakfast intake significantly improved TG concentration independent of resistance exercise. Our findings are supported by an earlier study, which showed that egg intake does not attenuate the positive lipid-altering effects of endurance exercise in untrained normolipidemic men and women. Taken together, these studies suggest that egg intake does not inhibit exercise induced improvements in blood lipid concentration, and it may serve as an advantageous addition to the dietary intake of recreationally trained individuals.

Ethnic-based and age-based differences in blood lipid concentrations definitely exist; therefore, it is imperative to determine the blood lipid response to egg intake across different cohorts. Eggs are a predominant part of the diet in Mexico, whose population is generally characterized by dyslipidemia and increased CVD risk. In Mexican children, adding two eggs per day to usual intake for 30 days did not change their LDL C/HDL-C ratio.

Interestingly, a shift toward the larger, less atherogenic LDL particle size was observed when compared with intake of a cholesterol-free (CF) egg substitute. A study conducted in healthy university students concluded that consumption of an egg-based breakfast (two eggs) five times per week for 14 weeks did not alter blood lipids when compared with an egg-free, calorie matched breakfast. Moreover, middle-aged men and premenopausal women (aged 20-50 y) who consumed three eggs per day for 30 days did not have alterations in their LDL-C or HDL-C. To further expand the evidence to wider age ranges, responses to egg feeding were assessed in postmenopausal women (≥60 y) and adults aged 40 to 65 years consuming three eggs and one egg per day, respectively. Similar to the studies described previously, no differences in LDL-C or HDL-C were observed. Overall, the evidence illustrates that adding eggs to normal dietary intake does not negatively alter blood lipid concentration and/or increase CVD risk across a range of ages and ethnicities.

**Egg Intake in Individuals at Increased Risk for CVD**

Cardiovascular disease is progressive, and various early chronic disease-related conditions (comorbidities) place an individual at increased risk for developing CVD. These modulating conditions such as obesity, insulin resistance, and metabolic syndrome (MetS) have become targets of CVD prevention research. Understanding that individuals with comorbidities are at an increased risk for CVD, it is important to critically evaluate the effects of egg intake on CVD risk factors in these populations. Following is a discussion of dietary intervention studies that have assessed the addition of eggs combined with moderate carbohydrate restriction to usual dietary intake in individuals with pre-existing heart conditions and/or at increased risk for CVD. Individuals who are obese and overweight (body mass index [BMI] >25 and <50 kg m²) are at increased risk for developing insulin resistance and MetS, which can independently or in combination lead to CVD. In a study that assessed the difference between implementing either an egg-based or bagel-based breakfast to usual dietary intake or during an energy deficit, low-fat diet (1000 kcal) in obese adults, no differences in blood lipid concentrations were observed regardless of group assignment. However, individuals following the egg-based, low-fat diet exhibited significantly decreased adiposity relative to those consuming the bagel-based,
low-fat diet. This study’s results suggest that the addition of eggs augmented the usual modulation in adiposity observed with an energy deficit. Furthermore, another study demonstrated that when three whole eggs per day for 12 weeks were added to a moderate carbohydrate-restricted diet in overweight/obese adult men, no difference in LDL-C was observed, whereas a significant increase in HDL-C occurred relative to a CF egg substitute. Moreover, in a dose-response (0, 2, or 4 eggs) crossover study, insulin-sensitive, insulin-resistant, and obese individuals all exhibited increased plasma HDL-C concentrations following consumption of four eggs per day for 4 weeks, while increased LDL-C was observed in both insulin-sensitive and insulin resistant individuals.

A significant contributor to increased CVD risk observed in MetS is the atherogenic dyslipidemia frequently associated with this condition, which can ultimately lead to impaired endothelial function. Most recently, egg intake (2/d) for 6 weeks did not modulate endothelial function in obese individuals with coronary artery disease, as measured by flow mediated dilation. Lipid modulating interventions have served as a desired target for improving MetS, thus decreasing CVD risk. Carbohydrate restricted diets have also served as an advantageous strategy for decreasing CVD risk, due to a propensity to decrease adiposity. With consideration of these variables, the addition of whole eggs to moderate CHO restriction (25%-30% energy) was applied, producing a significant increase in HDL-C along with decreases in TG, oxidized LDL, and very LDL-C, relative to a CF egg substitute in individuals with MetS. Moreover, the same group has demonstrated that individuals consuming whole eggs have significantly decreased tumor necrosis factor alpha (TNF-α) and C-reactive protein (CRP) relative to individuals consuming CF egg substitute. TNF-α and CRP are inflammatory cytokines commonly associated with obesity, insulin resistance, and MetS; thus, these cytokines may serve as a potential target for addressing the mechanism underlying the lipid modulating effects of eggs.

Egg-Induced Modulation of Lipoprotein Metabolism: Potential Mechanisms

HDL-C is a critical cardioprotective biomarker in metabolic disease, and decreased HDL-C places an individual at increased risk of developing CVD. HDL is thought to promote cardiovascular health by mediating acquisition of lipids from macrophage foam cells within the arterial wall for participation in reverse cholesterol transport, while the anti-inflammatory properties of HDL further protect against atherosclerosis. It is widely accepted that HDL function is impaired under inflammatory conditions, and steady-state blood HDL-C concentration may fail to completely demonstrate the true anti-atherogenic potential of this lipoprotein. Therefore, studies addressing the mechanistic function of HDL as a lipid acceptor and as a means of decreasing inflammation may be a better estimate of CVD risk than steady-state HDL-C alone.

Recently, when macrophages were incubated with serum collected from individuals consuming three eggs per day for 12 weeks, an increase in cholesterol-accepting capacity (increased serum HDL) was observed from baseline to 12 weeks, relative to serum from individuals consuming the equivalent amount of CF egg substitute. A follow-up study from the same group demonstrated that changes in cholesterol-accepting capacity might be due to an increase in lecithin-cholesterol acyltransferase (LCAT) activity, which serves to convert free cholesterol to cholesterol esters as part of the reverse cholesterol transport system. Moreover, the same study revealed that in the face of a known potent pro-inflammatory molecule (lipopolysaccharide [LPS]), serum from individuals consuming whole eggs elicited a protective effect on peripheral blood mononuclear cell inflammatory cytokine secretion, relative to serum from individuals consuming CF egg substitute.

As previously mentioned, egg yolks are a rich source of xanthophyll carotenoids, specifically lutein and zeaxanthin. Significant increases in the circulating plasma concentrations of carotenoids have also been observed following egg consumption, relative to a CF egg substitute. These carotenoids have previously been shown to protect against inflammation, oxidation, and atherosclerosis, which may suggest a role of eggs in promoting cardiovascular health. Although a cardioprotective mechanism of eggs has not been fully elucidated, it is becoming clear that eggs do not place healthy or diseased individuals at increased risk for CVD, and they may ultimately serve to decrease disease risk. Future research should focus on the effects of egg consumption on CVD risk in hyper-responders.

† Please note this is an inaccurate statement. AHA/ACC does not recommend a limit of 300 mg/day of cholesterol.

†† Actual cholesterol content of an egg, based on USDA Food Composition Tables, varies by size, ranging from 141 mg (small) to 234 mg (jumbo).

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