Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: a meta-analysis[1–3]

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ABSTRACT

Background: Several epidemiologic studies found no effect of egg consumption on the risk of coronary heart disease. It is possible that the adverse effect of eggs on LDL-cholesterol is offset by their favorable effect on HDL cholesterol.

Objective: The objective was to review the effect of dietary cholesterol on the ratio of total to HDL cholesterol.

Design: Studies were identified by MEDLINE and Biological Abstracts searches (from 1974 to June 1999) and by reviewing reference lists. In addition, we included data from a more recently published study. Studies were included if they had a crossover or parallel design with a control group, if the experimental diets differed only in the amount of dietary cholesterol or number of eggs and were fed for ≥14 d, and if HDL-cholesterol concentrations were reported. Of the 222 studies identified, 17 studies involving 556 subjects met these criteria.

Results: The addition of 100 mg dietary cholesterol/d increased the ratio of total to HDL cholesterol by 0.020 units (95% CI: 0.010, 0.030), total cholesterol concentrations by 0.056 mmol/L (2.2 mg/dL) (95% CI: 0.046, 0.065 mmol/L; 1.8, 2.5 mg/dL), and HDL-cholesterol concentrations by 0.008 mmol/L (0.3 mg/dL) (95% CI: 0.005, 0.010 mmol/L; 0.2, 0.4 mg/dL).

Conclusions: Dietary cholesterol raises the ratio of total to HDL cholesterol and, therefore, adversely affects the cholesterol profile. The advice to limit cholesterol intake by reducing consumption of eggs and other cholesterol-rich foods may therefore still be valid.   *Am J Clin Nutr* 2001;73:885–91.

KEY WORDS   Dietary cholesterol, eggs, total cholesterol, HDL cholesterol, LDL cholesterol, meta-analysis

INTRODUCTION

One of the dietary recommendations in the prevention of coronary heart disease is to limit egg consumption (1) because eggs have been shown to be a major source of dietary cholesterol (2). Dietary cholesterol increases serum total and LDL-cholesterol concentrations (3–7), which are established risk factors for coronary heart disease (8); however, several epidemiologic studies found no relation between egg consumption and risk of coronary heart disease (9, 10). The absence of such a relation may imply that the recommendation of lowering egg consumption is of little use in the prevention of coronary heart disease. One egg contains ≈200 mg/cholesterol. Although it is obvious that dietary choles-

terol increases total cholesterol concentrations (3, 6, 7), several studies showed that dietary cholesterol increases not only concentrations of LDL cholesterol but also concentrations of HDL cholesterol (3, 6). Because HDL cholesterol may protect against coronary heart disease, the adverse effects of egg consumption on total and LDL-cholesterol concentrations might be attenuated by the favorable effects on HDL-cholesterol concentrations.

The ratio of total to HDL cholesterol involves the opposing effects of LDL and HDL cholesterol on coronary heart disease risk. As a result, the ratio is a better predictor of coronary heart disease risk than are individual lipoprotein concentrations (8, 11, 12). Therefore, it may be more appropriate to study the effect of dietary cholesterol on the ratio of total to HDL cholesterol than on individual lipoprotein concentrations.

We reviewed well-controlled studies to study the effect of dietary cholesterol from egg intake on the ratio of total to HDL-cholesterol concentrations in humans. We added data from an unpublished study of our own.

METHODS

Selection of studies

We screened MEDLINE (National Library of Medicine, Bethesda, MD) from 1974 through June 1999 and Biological Abstracts from 1989 through June 1999 for experimental studies on the effects of dietary cholesterol and eggs on total cholesterol and lipoproteins. We did not screen MEDLINE before 1974 because measurements of HDL cholesterol, which were part of our main outcome measure, were not available at that time. For the literature searches, the key words *egg*, *eggs*, and *dietary cholesterol* were each intersected with the words serum (plasma) *lipoprotein*, *serum* (*plasma*) *cholesterol*, *HDL*, and *LDL*. We found 1190 citations in MEDLINE and 883 in Biological

TABLE 1
Characteristics of studies and diets and the effects of dietary cholesterol on serum cholesterol and lipoproteins[1]

Reference	Design	Subjects	No. of subjects per group	Diet characteristics			Changes in serum cholesterol				
				Change in cholesterol	Energy	P:S	Total	HDL	LDL	Total: HDL	HDL: LDL
				mg/d	*MJ*		*mmol/L*				
Chenoweth et al, 1981 (15)	X[2]	Controlled (*n* = 32 M)	16[3]	554	12.5	0.52	0.54	0.09	0.37	0.20	−0.01
			16	542	12.9	1.22	0.35	0.02	0.22	0.15	−0.02
Buzzard et al, 1982 (16)	//[4]	Free-living (*n* = 20 M)	10	563	—	—	0.27	−0.05	—	0.36	—
			10(c)[5]	0	—	—	0.15	−0.02	—	0.08	—
Applebaum-Bowden et al, 1984 (17)	X	Controlled (*n* = 6 M, 3 F)	—	897	9.6	0.82	0.29	0.00	0.29	0.18	−0.05
Sacks et al, 1984 (18)	X	Free-living (*n* = 4 M, 13 F)	—	321	7.7	0.57	0.19	−0.08	0.29	0.25	−0.09
Flynn et al, 1986 (28)	X	Free-living (*n* = 54 M, 16 F)	—	682	8.6	—	0.41	0.04	—	0.19	—
Bowman et al, 1988 (19)	//	Controlled (*n* = 14 M)	7	294	11.8	0.42	0.02	−0.03	0.08	0.07	−0.03
			7(c)[5]	0	11.8	0.40	−0.13	0.00	−0.05	−0.09	0.01
Johnson and Greenland, 1990 (20)	X	Controlled (*n* = 10 M)	—	400	—	1.5	0.26	0.03	0.24	0.10	−0.04
Vorster et al, 1992 (21)	//	Free-living (*n* = 70 M)	19	167	13.5	0.7	0.06	0.03	0.15	−0.04	−0.01
			25	408	14.6	0.7	0.24	−0.01	0.16	0.22	−0.03
			26(c)[5]	30	14.0	0.8	−0.16	−0.02	−0.15	−0.07	0.02
Duane, 1993 (22)	X	Controlled (*n* = 12 M)	—	825	—	—	0.31	0.02	0.39	0.20	−0.02
Martin et al, 1993 (23)	X	Controlled (*n* = 30 M)	—	783	13.7	0.39	0.61	0.09	0.51	0.23	−0.06
Ginsberg et al, 1994 (24)	X	Controlled (*n* = 24 M)	—	215	9.4	0.78	0.14	−0.01	0.19	0.16	−0.04
				430	9.4	0.78	0.16	−0.01	0.17	0.17	−0.04
				860	9.4	0.78	0.29	0.03	0.30	0.15	−0.04
Ginsberg et al, 1995 (25)	X	Controlled (*n* = 13 F)	—	169	7.6	0.87	0.16	0.04	0.10	0.03	−0.01
				559	7.6	0.86	0.42	0.09	0.31	0.10	−0.05
Knopp et al, 1997 (30)	//	Free-living (*n* = 55 M, 24 F)	44	467	8.0	0.71	0.15	0.10	0.07	−0.24	0.02
			35(c)[5]	−30	8.1	0.82	0.07	0.02	−0.01	−0.02	0.01
	//	Free-living (*n* = 31 M, 21 F)	31	467	8.0	0.71	0.31	0.08	0.32	−0.13	0
			21(c)[5]	−30	8.1	0.82	0.21	0.02	0.12	0.08	0
Blanco-Molina et al, 1998 (26)	X	Controlled (*n* = 15 M)	—	457	11.2	0.54	0.31	0.01	0.19	0.22	−0.04
Romano et al, 1998 (29)	X	Free-living (*n* = 11 M)	—	800	—	—	0.46	0.09	0.31	0.06	0.00
	X	Free-living (*n* = 10 M)	—	800	—	—	0.29	0.03	0.46	0.15	−0.04
Sehayek et al, 1998 (27)	X	Controlled (*n* = 10 M, 8 F)	—	335	11.7	0.35	0.30	−0.03	0.30	0.28	−0.07
Weggemans et al, 2000 (31)	X	Controlled (*n* = 14 M, 36 F)	—	803	11.0	0.40	0.55	0.11	0.43	0.15	−0.05

[1] To convert serum lipid values from mmol/L to mg/dL, divide by 0.02586. P:S, ratio of polyunsaturated to saturated fat.

[2] X, crossover design or Latin-square design.

[3] The 32 subjects were distributed over 2 crossover studies; thus, there were 16 subjects per study.

[4] //, parallel design.

[5] Control subjects.

Abstracts. In addition, we checked the reference lists of several meta-analyses (3, 6, 7, 13, 14) and selected studies. A scan of the titles led to the selection of 221 citations. The abstracts of these citations were examined for compliance with the following inclusion criteria: *1*) studies had to be published in English; *2*) within a study, the composition of the experimental diets could differ only by the amount of cholesterol or the amount of eggs; *3*) subjects had to be weight stable throughout the study; *4*) the design had to eliminate the effect of nonspecific drifts of the outcome variable with time, which have been accomplished either by feeding different groups of volunteers different diets side by side (parallel design) or feeding each volunteer several diets in random order (crossover or Latin-square design); *5*) feeding periods had to be ≥14 d to attain equilibrium in concentrations of total cholesterol and lipoproteins; and *6*) studies had to report fasting concentrations of total cholesterol and lipoproteins. Studies with before-and-after designs or linear designs without a control group were excluded.

Of the 221 articles passing the title scan, 56 passed the abstract scan. Because most of the 56 abstracts did not provide sufficient information on the basis of our selection criteria, we checked the full text of these articles. Sixteen of the 56 articles (28%) met the inclusion criteria (15–30). Most other studies were not selected because they did not provide information on HDL-cholesterol concentrations or had a linear design without a control group. In addition to the data of these 16 studies, we used data from our own recent study on the response to egg yolk cholesterol as a function of the apolipoprotein A4 1/2 polymorphism (31) (**Table 1**).

The 17 selected studies yielded 24 dietary comparisons and 5 control treatments. The studies included 422 men and 134 women. Ten studies were conducted with men only, 6 included both men and women, and 1 included only women. No studies reported the race of the subjects. The age of the volunteers ranged from 18 to 75 y, mean body mass index (in kg/m^2) ranged from 20.8 to 28, and mean baseline cholesterol concentration ranged from 4.06 to 5.92 mmol/L (157 to 229 mg/dL). Not all studies reported mean body mass index (15, 17–19, 22, 28) or baseline cholesterol concentration (22, 23, 27, 30). There were 11 metabolic ward studies, in which all food was provided; 5 of these studies were of

free-living subjects who were provided eggs, high cholesterol products, or egg-free substitutes. The change in cholesterol intake ranged from 137 to 897 mg/d. Values for total, LDL-, and HDL-cholesterol plasma concentrations were multiplied by 1.029 to convert to serum values (32).

Statistical analysis

We subtracted the mean concentration of serum cholesterol at the end of the low-cholesterol diet from that at the end of the high-cholesterol diet to calculate the change in serum cholesterol. Six studies reported the means of individual ratios of total to HDL cholesterol (17, 20, 22, 26, 31, 33) and 4 studies reported the means of the individual ratios of HDL- to LDL-cholesterol concentrations (17, 22, 29, 31). Therefore, we used mean concentrations of total, LDL, and HDL cholesterol at the end of each diet to estimate the mean ratios of total to HDL- cholesterol and of HDL- to LDL-cholesterol concentrations. Ratios have larger variation than do individual cholesterol and lipoprotein concentrations. According to the Taylor approximation, this procedure to calculate the ratios causes an underestimation of the true ratio. The size of the underestimation is dependent on the total variation in the numerator and denominator and the correlation between the numerator (x) and denominator (y) as follows:

$$E(x/y) \approx \{E(x)/E(y) \times (1 + CVy \times [CVy - Corr\ (x,y) \times CVx])\} \quad (1)$$

where $E(x/y)$ is the expected mean value of x/y, $E(x)$ is the expected mean value of x, $E(y)$ is the expected mean value of y, and Corr (x,y) is the correlation between x and y (34). From an independent and large set of data (35), we calculated the CV's of total cholesterol (0.21), HDL cholesterol (0.22), and LDL cholesterol (0.25), and the correlation coefficients of HDL cholesterol with total cholesterol (0.194) and with LDL cholesterol (0.195). Therefore, the ratio of mean total cholesterol to mean HDL cholesterol that we used was ≈4% lower than the mean of the individual ratios. Similarly, the ratio of mean HDL to mean LDL cholesterol was ≈7% lower. We assumed that the underestimation varied at random by treatment and study. This implies that ratio changes in the present study are marginally smaller than those obtained when the mean change in individual ratios were used. We did not adjust the ratios and their changes for this minute underestimation.

For studies with a crossover or Latin-square design, the observed changes could be attributed fully to the change in dietary cholesterol or egg consumption because the study design eliminates drift of variables over time. For studies with a parallel design, we adjusted for the drift of variables over time by subtracting the changes in total cholesterol and lipoproteins in the control group from those in the treatment group. For instance, with a 563-mg/d increase in cholesterol intake in one study, total cholesterol concentrations increased by 0.27 mmol/L (10.4 mg/dL) in the treatment group and by 0.15 mmol/L (5.8 mg/dL) in the control group (16). We subtracted the 0.15 mmol/L (5.8 mg/dL) from the 0.27 mmol/L (10.4 mg/dL) to obtain the actual increase in the treatment group, which was 0.12 mmol/L (4.6 mg/dL).

Regression analysis

We used linear regression models (General Linear Models procedure; 36) to study the effect of dietary cholesterol on total cholesterol and lipoproteins. We did not use nonlinear regression models because the number of studies in our data set was limited. Furthermore, the present analysis was of only 3 studies

(17, 22, 23) involving subjects with a cholesterol intake just >1000 mg dietary cholesterol/d, whereas the relation between cholesterol intake and cholesterol concentrations appears linear when cholesterol intake is ≤1000 mg dietary cholesterol/d (7). We applied several linear models. In one model, the change in total cholesterol and lipoproteins (mmol/L) was expressed as a function of the absolute change in dietary cholesterol in mg/d. Regression lines were forced through the origin because a zero change in cholesterol intake will by definition produce no change in lipoprotein cholesterol concentrations attributable to dietary cholesterol. Thus, we applied the model described below.

$$\text{Change in serum cholesterol} = \beta \times (\text{change in dietary cholesterol}) \quad (2)$$

where the change in serum cholesterol is expressed in mmol/L for concentrations and in dimensionless units for ratios. The change in dietary cholesterol is expressed in units of 100 mg dietary cholesterol/d.

We also expressed dietary cholesterol in mg/MJ (1 MJ = 238 kcal). For these analyses, we excluded 4 studies that did not provide data on energy intake (16, 20, 22, 29). There were no large differences in average energy intake among the various studies and the results were not materially altered when we expressed dietary cholesterol in mg/MJ instead of mg/d. Therefore, we only report the effects of a change in dietary cholesterol in mg/d.

Although studies were selected on the basis of the design and duration of treatments, there were still considerable differences among the studies. The number of subjects per study ranged from 9 to 131. To account for this, it is common in meta-analyses to weigh each study by the reciprocal of the squared SE. However, the SEs of the changes in cholesterol and lipoprotein concentrations were not reported in some studies. We therefore weighed each study by the number of subjects, which is inversely proportional to the squared SE. Further, the ratio of polyunsaturated to saturated fat of the background diet varied among studies. A high ratio of polyunsaturated to saturated fat, which is an indicator of a background diet relatively low in saturated fat, may attenuate the change in total cholesterol after an increase in dietary cholesterol (7, 37, 38). In additional analyses we checked whether the ratio of polyunsaturated to saturated fat affected the relation of dietary cholesterol with total cholesterol and lipoproteins. Analysis of the residuals was performed to check the appropriateness of each model.

To detect publication bias, we explored heterogeneity in funnel plots visually. Hereto, we plotted the response of serum lipids to 100 mg dietary cholesterol against the sample size by study. In the absence of bias, the plots will resemble a symmetrical inverted funnel, as results of small studies will scatter at the left side of the plot with the spread narrowing among larger studies on the right side of the plot (39).

RESULTS

All 17 studies reported values for total and HDL cholesterol, but 2 studies did not report values for LDL cholesterol (Table 1; 16, 21). Most studies presented comparisons of 2 diets, but 4 studies presented comparisons of 3 or 4 diets (15, 21, 24, 25). In 2 studies, various groups of subjects were studied side by side. In one study, diabetics were compared with healthy subjects (29), whereas in another study hyperlipemic subjects were compared with subjects with familial-combined hyperlipemia (30).
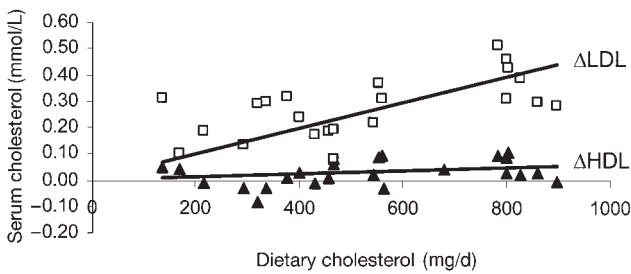
FIGURE 1. Changes in serum LDL-cholesterol (□) and HDL-cholesterol (▲) concentrations with cholesterol intake in 17 studies providing 24 dietary comparisons.

The ratio of total to HDL cholesterol and the concentrations of total and LDL cholesterol increased relative to control groups or treatments after an increase in dietary cholesterol in all but one of the studies, whereas HDL cholesterol concentrations increased in 19 of the 24 dietary comparisons. The ratio of HDL- to LDL-cholesterol concentrations decreased in all but one of the studies.

If we assume that one egg contains 200 mg/cholesterol (2), consuming one additional egg daily will increase the ratio of total to HDL cholesterol by 0.041 ± 0.011 units ($\overline{x}$ ± SEE), total cholesterol by 0.111 ± 0.010 mmol/L (4.3 ± 0.4 mg/dL), LDL cholesterol by 0.100 ± 0.008 mmol/L (3.9 ± 0.3 mg/dL), and HDL cholesterol by 0.016 ± 0.003 mmol/L (0.6 ± 0.1 mg/dL) (**Figure 1**). One additional egg daily will decrease the ratio of HDL- to LDL cholesterol by 0.011 ± 0.002 units (**Table 2**).

We then divided the studies into 2 groups: those with a polyunsaturated-to-saturated fat ratio ≤ 0.7, indicative of a background diet relatively high in saturated fat, and those with a ratio > 0.7, indicative of a background diet relatively low in saturated fat. The response of LDL-cholesterol concentrations to a change in dietary cholesterol was somewhat weaker in the studies with a background diet low in saturated fat than in those with a background diet high in saturated fat (**Figure 2**). We estimated that each additional 100 mg dietary cholesterol would increase serum LDL cholesterol by 0.036 ± 0.004 mmol/L in the studies with a background diet low in saturated fat and by 0.061 ± 0.006 mmol/L in the studies with a background high in saturated fat ($P = 0.03$). The fatty acid composition of the background diet did not affect the response of HDL-cholesterol concentrations to dietary cholesterol or the ratios of total to HDL-cholesterol or of HDL- to LDL-cholesterol concentrations.

We did not detect publication bias as indicated by the absence of heterogeneity in funnel plots (results not shown). We checked whether our results could also be applied to other studies. For this purpose, we selected 19 articles that reported HDL-cholesterol concentrations but had failed to meet other inclusion criteria, eg, design. These 19 studies provided 33 dietary comparisons (38, 40–57). In 20 of these 33 dietary comparisons, the ratio of total to HDL-cholesterol concentrations increased, whereas in the other 13 comparisons the ratio decreased when cholesterol intake increased. Regression analysis showed that an increase of 100 mg dietary cholesterol/d increased the ratio of total to HDL cholesterol by 0.014 ± 0.003 units in these studies, whereas the ratio was increased by 0.020 units in the studies that fulfilled our selection criteria (**Figure 3**).

DISCUSSION

Our meta-analysis of 17 trials showed that dietary cholesterol increased the ratio of total to HDL-cholesterol concentrations. The effect was highly significant ($P < 0.0009$) and the 95% CI was narrow. This suggests that the favorable rise in HDL cholesterol with increased cholesterol intake fails to compensate for the adverse rise in total and LDL-cholesterol concentrations and, therefore, that increased intake of dietary cholesterol may raise the risk of coronary heart disease. Our meta-analysis included men and women with a wide age range from North America (15–20, 22–25, 28, 30), Europe (26, 27, 29, 31), and South Africa (21). The narrow CIs (Table 2) indicate that, although only 24 points were assessed, the effect of dietary cholesterol on serum cholesterol and lipoproteins was repeatable in different studies and populations. The consistency of the findings among studies suggests that our conclusions are valid for much of the white populations of affluent countries. However, the absence of data on the race of subjects does not allow for a confident extrapolation to other populations.

In the present study, we used a regression model without an intercept because no change in cholesterol intake will by definition produce no change in the serum cholesterol concentration that could be attributed to dietary cholesterol. However, in those studies that alter the intake of eggs, the intake of dietary cholesterol, and of other egg components that may affect the serum cholesterol concentration, such as fat and lecithin, is changed. These factors may also affect concentrations of serum cholesterol and, thus, for such studies it may not be valid to force the regression line through the origin. To check this, we performed an analysis excluding studies that altered the intake of eggs (16, 18, 21, 28) or did not report whether the change in fat intake was adjusted for in the control diet (22, 26). This did not materially alter the results and thus we included these studies in our analysis.

Stratification of the studies for study design (crossover or Latin-square compared with parallel), setting (metabolic ward compared with free-living), or adjustment of the change in dietary cholesterol for energy intake did not materially alter the results. A high polyunsaturated-to-saturated fat ratio, indicating a background diet relatively low in saturated fat, attenuated the change in LDL-cholesterol concentration induced by an increase in dietary cholesterol. Some other studies also found that a background diet low in saturated fat attenuated the effect of dietary cholesterol on serum total cholesterol and LDL-cholesterol concentration (37, 38, 58), whereas other studies did not (15, 33, 44, 52, 59–61). In some of the latter studies the change in dietary cholesterol might have been too small to show an effect of the fat composition of the background diet on the change in serum cholesterol concentration. The polyunsaturated-to-saturated fat

TABLE 2
Predicted changes in serum total cholesterol concentration and lipoproteins induced by a 100-mg/d increase in dietary cholesterol[1]

Serum cholesterol concentration	Predicted change (95% CI)
Total cholesterol (mmol/L)	0.056 ± 0.005 (0.046, 0.065)
HDL cholesterol (mmol/L)	0.008 ± 0.001 (0.005, 0.010)
LDL cholesterol (mmol/L)	0.050 ± 0.004 (0.042, 0.058)
Total:HDL cholesterol	0.020 ± 0.005 (0.010, 0.030)
HDL:LDL cholesterol	−0.006 ± 0.001 (−0.008, −0.004)

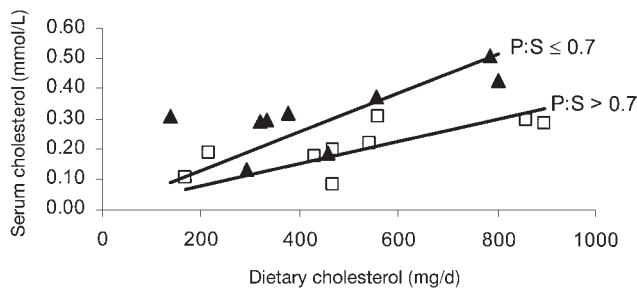[1] $\overline{x}$ ± SEE. To convert serum lipid values from mmol/L to mg/dL, divide by 0.02586.

FIGURE 2. The effect of a change in cholesterol intake on serum LDL cholesterol in studies with a ratio of polyunsaturated to saturated fat ≤0.7 (▲) and >0.7 (□).

ratio, however, does not take into account the absolute amount of fat in a diet. Thus, a diet with 5% of energy from polyunsaturated fat and 10% of energy from saturated fat has the same ratio as a diet with 10% of energy from polyunsaturated fat and 20% of energy from saturated fat. Differences between studies in the absolute amount of fat may therefore also serve as an explanation for some of the inconsistent results.

We found no publication bias in our meta-analysis by use of funnel plots. In the studies that failed to fulfill our selection criteria, the effect of dietary cholesterol on the ratio of total to HDL cholesterol was somewhat smaller than in those included in our meta-analysis. This might be due to a lack of dietary control resulting in a large error in the amount of dietary cholesterol that was changed. This attenuates the estimated effect of dietary cholesterol on serum cholesterol concentration toward the null (62). However, it may also be due to the lack of adjustment for the change in fat intake that is induced by the change in egg consumption. Only 3 (42, 48, 51) of these 19 studies adjusted for the change in fat intake, whereas 11 of the 17 studies included in our meta-analysis accounted for the change. Nevertheless, the effect of dietary cholesterol on the ratio of total to HDL cholesterol in the studies that failed to fulfill our selection criteria leaned in the same direction as the effect in our meta-analysis. This indicates that the present results are not due to a biased selection of the studies.

Effects in hyperlipemic subjects

Cholesterol-lowering diets are usually prescribed to hyperlipemic subjects with total cholesterol concentrations >5.0 mmol/L (193 mg/dL) (63). However, the mean baseline cholesterol concentrations of subjects in the studies that fulfilled our selection criteria were <5.0 mmol/L (193 mg/dL), except for 2 studies (15, 30). The moderately hyperlipemic subjects in the study of Chenoweth et al (15) showed a 0.15- or 0.20-unit increase in the ratio of total to HDL cholesterol after an increase in dietary cholesterol, whereas the hyperlipemic subjects in the study of Knopp et al (30) showed a 0.22-unit decrease and the subjects with familial combined hyperlipemia showed a 0.21-unit decrease with an increase in dietary cholesterol of 437 mg/d. In the latter study, the percentage increase in the HDL-cholesterol concentration was larger than that in the total cholesterol concentration. The opposite effect between the studies may have been a chance finding due to the large day-to-day variation in cholesterol concentrations. The additional analysis

with studies that failed to fulfill our selection criteria included 5 studies with mostly moderately hyperlipemic subjects (41, 52, 53, 55, 56). Because of the limited number of studies, we could not analyze these studies separately. Nevertheless, the results of these studies did not clearly differ from those in subjects with normal cholesterol concentrations. Therefore, the results of the present meta-analysis appear also to be applicable to hyperlipemic subjects.

Effects on total cholesterol and LDL-cholesterol concentrations

The estimated change in total cholesterol was 0.056 mmol/L (2.2 mg/dL) for each 100-mg/d increase in dietary cholesterol. The predicted change is somewhat smaller than the change of 0.064 mmol total cholesterol/L predicted by the formula of Keys and Parlin (5) assuming a change in dietary cholesterol from 300 to 400 mg/d and is considerably smaller than the change of 0.175 mmol total cholesterol/L predicted by the formula of Hegsted et al (4), but agrees well with changes estimated from more recent meta-analyses (3, 6, 7, 14). It is suggested that a simple linear model may predict group mean changes in LDL-cholesterol concentrations rather well over the normal range of dietary cholesterol intakes, as shown in Figure 1. Because diet-induced changes in total cholesterol and lipoproteins vary considerably between individuals (42, 64, 65), our results cannot reliably predict changes in total cholesterol and lipoproteins in individual subjects or patients.

Dietary cholesterol and risk of coronary heart disease

We showed that consuming one additional egg daily will increase the ratio of total to HDL-cholesterol concentrations by 0.040 units, which would imply an increase in the risk of myocardial infarction of 2.1% (11). The calculated increase in risk may be small in an individual patient, but in view of the widespread consumption of diets high in cholesterol it may be substantial at the population level.

Of course, these calculations do not take into account the effects of other nutrients in eggs that may be beneficial in preventing coronary heart disease, eg, vitamin E, folate, other B vitamins, and unsaturated fatty acids (2). Hu et al (10) calculated that in the United States, eggs contribute to the intake of many nutrients, such as retinol (4%), α-tocopherol (3%), folate (4%), other
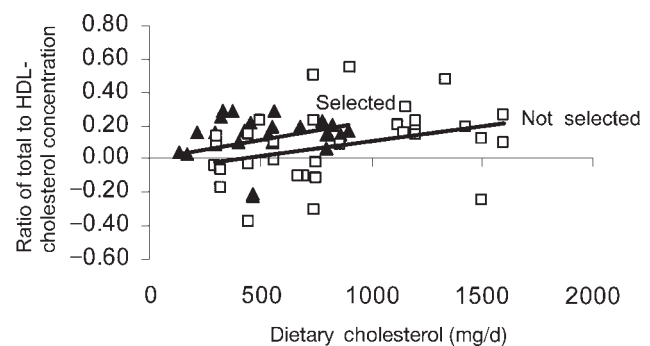

FIGURE 3. The effect of an increase in dietary cholesterol on the ratio of total cholesterol to HDL cholesterol in 17 studies that fulfilled the selection criteria (▲) and 19 studies that did not fulfill our selection criteria (□).

B vitamins (≤3%), monounsaturated fat (3%), and linoleic acid (2%); however, eggs contributed to 32% of total dietary cholesterol. Thus, in view of the relatively small contribution of eggs to the intake of nutrients that may be beneficial in preventing coronary heart disease, the recommendation to limit the consumption of eggs may still be valid for the prevention of coronary heart disease. Other major sources of dietary cholesterol are dairy fats and meat, but these are already considered as increasing the risk of heart disease because of their saturated fat content.

In conclusion, the consumption of cholesterol increases the ratio of total to HDL-cholesterol concentrations, which would predict increased risk of coronary heart disease. Therefore, the advice to limit the consumption of eggs and other foods rich in dietary cholesterol may still be important in the prevention of coronary heart disease.

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