식이 콜레스테롤 제한 없애도 좋은가?

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USDA

Scientific Report of the 2015 Dietary Guidelines Advisory Committee

Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture

Nutrients of concern for overconsumption

Cholesterol. Previously, the Dietary Guidelines for Americans recommended that cholesterol intake be limited to no more than 300 mg/day. The 2015 DGAC will not bring forward this recommendation because available evidence shows no appreciable relationship between consumption of dietary cholesterol and serum cholesterol, consistent with the conclusions of the AHA/ACC report.[2,35] Cholesterol is not a nutrient of concern for overconsumption.

Cardiovascular disease and Risk factors

- Cardiovascular disease; leading cause of and mortality
  - Risk factors; age, blood pressure, smoking, diabetes, dyslipidemia
  - A preventable cause of death
- Dyslipidemia
  - High TC, high LDL, high TG, low HDL levels in plasma
  - Diet is an important determinant of plasma lipid levels
    ; percentage of fat calorie, fatty acids, cholesterol, fiber, plant sterol

Correlation between dietary factors and CHD mortality

- Epidemiologic data (25-year CHD mortality in 7 countries)

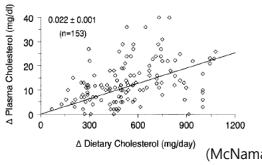
	SFA	Serum CHOL	CHD
Serum CHOL	0.71**	***	0.73**
C12:0	0.83***	0.84***	0.84***
C14:0	0.88***	0.81***	0.86***
C16:0	0.97***	0.62*	0.81***
C18:0	0.97***	0.60*	0.84***
SFA	***	0.71**	0.88***
C18:1C	0.05	0.17	−0.08
C18:1T	0.84***	0.70**	0.78***
C18:2CC	0.30	−0.06	0.00
EPA + DHA (log)	−0.51*	−0.26	−0.36
Dietary CHOL	0.62*	0.46	0.55*
Total fat	0.80***	0.62*	0.60*
Energy	0.29	0.09	0.28

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. (Kromhout et al. Prev Med 1995; 24:308)

- Confounding factors need to be considered

Dietary Cholesterol leads to high blood cholesterol?

- Meta-analysis on 153 human CH feeding trials
- Positive correlation between CH intake and plasma CH



(McNamara, J Am Coll Nutr 2000;19(5):540S)

- Dietary CH increases both LDL and HDL
  ; Addition of 100mg CH leads to increase of plasma TC 2.2 mg/dl, LDL 1.9mg/dl, HDL 0.4mg/dl

- Weighted multiple-regression analysis on 224 studies

Correlations between changes in dietary variables and corresponding changes in blood lipid response variables[1]

	ΔSerum total cholesterol (μmol/L)	ΔVLDL (μmol/L)	ΔLDL (μmol/L)	ΔHDL (μmol/L)	ΔTriacylglycerol (μmol/L)
ΔCholesterol (mg/d)					
r^2	0.502	0.050	0.463	0.358	−0.013
n^3	307	61	185	225	218
P	< 0.0005	0.704	< 0.0005	< 0.0005	0.852
ΔFat (% of energy)[4]					
r	0.423	−0.201	0.523	0.579	−0.091
n	345	65	194	237	233
P	< 0.0005	0.109	< 0.0005	< 0.0005	0.166
ΔPUFA (% of energy)					
r	−0.624	−0.371	−0.479	−0.237	−0.401
n	221	39	117	146	135
P	< 0.0005	0.020	< 0.0005	0.004	< 0.0005
ΔMUFA (% of energy)					
r	0.177	−0.060	0.120	0.251	−0.116
n	191	32	107	127	123
P	0.014	0.747	0.219	0.004	0.203
ΔSFA (% of energy)					
r	0.803	0.051	0.790	0.604	−0.020
n	244	40	129	169	155
P	< 0.0005	0.755	< 0.0005	< 0.0005	0.807

$$\Delta\text{Serum total cholesterol (mg/dL)} = 1.918 \cdot \Delta\text{SFA} - 0.900 \cdot \Delta\text{PUFA} + 0.0222 \cdot \Delta\text{cholesterol}$$

(Howell et al. AJCN 1997;65:1747)

Dietary Cholesterol from Eggs Increases Plasma HDL Cholesterol in Overweight Men Consuming a Carbohydrate-Restricted Diet[1,2]

- Dietary CH intervention (640mg, 0mg) with low carbohydrate (10-15% E) diet for 12 wks (n=28, BMI 25~37, aged 40~70y)
  ; increases plasma HDL without effect on LDL and TC

Variable	Baseline	Wk 6	Wk 12	Mean absolute change	*P*-value (Time)
Total cholesterol,[2] *mg/dL*				*unit/12 wk*	
EGG	198.3 ± 42.1	194.5 ± 40.6	202.2 ± 41.8	+3.9	
SUB	188.3 ± 33.7	178.7 ± 33.1	187.3 ± 39.5	+1.0	>0.1
TG,[3] *mg/dL*					
EGG	114.2 ± 49.4	72.7 ± 20.7	70.1 ± 20.8	−44.1	
SUB	126.1 ± 69.4	91.9 ± 31.3	76.7 ± 33.0	−49.4	<0.001
HDL-C,[3] *mg/dL*					
EGG	47.6 ± 15.1[b]	59.6 ± 14.5[a]	57.1 ± 15.1[a]	+12.0	
SUB	50.0 ± 9.7[b]	49.4 ± 8.8[b]	48.8 ± 8.8[b]	−1.2	<0.01
LDL-C, *mg/dL*					
EGG	127.5 ± 42.2	121.2 ± 40.0	144.3 ± 45.1	+16.8	
SUB	110.8 ± 34.5	107.3 ± 34.4	121.5 ± 42.0	+13.5	>0.1
LDL-C/HDL-C					
EGG	2.27 ± 0.83	1.89 ± 0.75	2.46 ± 1.04	+0.19	
SUB	2.37 ± 1.14	2.23 ± 0.85	2.42 ± 0.78	+0.05	>0.25

Mutungi et al. J Nutr 2008; 138:272

Indian J Physiol Pharmacol 2004; 48 (3) : 286–292

THE EFFECT OF INGESTION OF EGG ON THE SERUM LIPID PROFILE OF HEALTHY YOUNG INDIANS

- Dietary CH intervention (300mg, 0 mg) with lacto-vegetarian diet for 8wks (n=34 , BMI 18~23, average age 25.7 years)
  ; No significant differences in TC, LDL, HDL, TG
  ; considerable variability among subjects

Parameter	*After control (egg free diet) treatment*	*After experimental (egg consumption) treatment*	
		4 wk	*8 wk*
Total cholesterol	183.72±27.90	189.84±24.55	191.84±29.63
LDL cholesterol	104.73±29.81	112.34±26.20	115.42±32.47
HDL cholesterol	52.54±12.43	51.95±11.43	50.05±11.82
VLDL cholesterol	25.33±7.32	25.65±8.59	27.36±9.07
Total triglycerides	114.54±30.73	116.71±33.61	120.50±35.61
Total cholesterol/HDL ratio	3.73±1.24	3.85±1.11	4.07±1.31*

- Secondary analysis after dividing subjects into 2 groups
  (less or greater than15% change in LDL in response to one egg per day)
  ; hyperresponders had a higher TC, LDL, TC/HDL

Serum lipid profile after control and experimental treatment in hyperresponders.

Parameter	*After control (egg free diet) treatment*	*After experimental (egg consumption) treatment*	
		4 wk	*8 wk*
Total cholesterol	172.42±24.73	191.18±27.89*	204.10±28.42*
LDL cholesterol	90.34±26.36	113.72±27.75*	127.89±31.77*
HDL cholesterol	54.20±13.87	51.53±11.78	47.66±12.72
VLDL cholesterol	26.85±8.67	25.60±9.90	26.03±11.46
Total triglycerides	126.19±41.58	126.06±43.76	128.04±49.08
Total cholesterol/HDL ratio	3.42±1.32	3.94±1.33	4.55±1.40*

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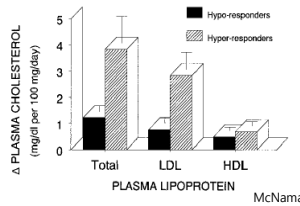
LDL cholesterol	104.73±29.81	112.34±26.20	115.42±32.47
HDL cholesterol	52.54±12.43	51.95±11.43	50.05±11.82
VLDL cholesterol	25.33±7.32	25.65±8.59	27.36±9.07
Total triglycerides	114.54±30.73	116.71±33.61	120.50±35.61
Total cholesterol/HDL ratio	3.73±1.24	3.85±1.11	4.07±1.31*

Individual variability in response to dietary cholesterol

- The difference in response to dietary CH
  (hypo-responder, hyper-responder)
- 15~25% of the population is sensitive to dietary CH
- Characteristics of hyper-responders to dietary CH
  ; combined hyperlipidemia, excess body weight, specific apoB, gene polymorphism (ABCG5/8, apo A-IV-2, NPC1L1, apo C-4..)



McNamara, J Am Coll Nutr 2000;19(5):540S

Am J Clin Nutr 2004;80:855–61.

Dietary cholesterol does not increase biomarkers for chronic disease in a pediatric population from northern Mexico[1–3]

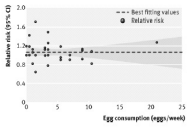
- Dietary CH intervention (518 mg, 0 mg) for 30d without controlling diet (n=54 ,8-12 y)
- Dividing subjects into 2 groups
  (change in TC from baseline less or greater than 0.05 mmol/L)
  ; hyper-responders had a higher LDL, HDL, but not TG and apoB
- Supplemental eggs increased mean LDL peak diameter

	LDL cholesterol	HDL cholesterol	TG	TC:HDL	Apo B	LDL peak diameter
	mmol/L	*mmol/L*	*mmol/L*	*mmol/L*	*mg/L*	*nm*
Hyperresponders						
EGG	1.93 ± 0.36[a]	1.35 ± 0.29[a]	1.00 ± 0.68	2.85 ± 0.57	606 ± 96	26.51 ± 0.10
SUB	1.54 ± 0.38[b]	1.23 ± 0.26[b]	1.02 ± 0.37	2.66 ± 0.52	598 ± 126	26.10 ± 0.11
Hyporesponders						
EGG	1.88 ± 0.42[a]	1.28 ± 0.19[a,b]	0.93 ± 0.31	2.96 ± 0.55	583 ± 106	26.32 ± 0.09
SUB	1.83 ± 0.44[a]	1.22 ± 0.19[b]	1.10 ± 0.47	3.00 ± 0.53	627 ± 109	26.19 ± 0.09
Diet effect	P < 0.0001	P < 0.001	NS	NS	NS	P < 0.01
Responder effect	P < 0.001	P < 0.001	NS	NS	NS	NS
Interaction	P < 0.01	P < 0.05	NS	NS	NS	NS

BMJ 2013;346:e8539 doi: 10.1136/bmj.e8539 (Published 7 January 2013)

Egg consumption and risk of coronary heart disease and stroke: dose-response meta-analysis of prospective cohort studies

- Meta-analysis on 8 reports (1966-2012) studying relative risk with 95% CI
- Increased risk of CHD among diabetic patients with higher egg consumption



Dose-response analyses of egg consumption and risk of coronary heart disease

	No of reports*	Relative risk (95% CI)	P for heterogeneity	I^2	P for test
Coronary heart disease					
Total cases	9	0.99 (0.85 to 1.15)	0.97	0.0	0.88
Fatal cases	4	1.18 (0.71 to 1.96)	0.91	0.0	0.53
Coronary heart disease with diabetes†	5	1.54 (1.14 to 2.09)	0.59	0.0	0.01
Stroke					
Total stroke	8	0.91 (0.81 to 1.02)	0.46	0.0	0.10
Fatal stroke	4	0.94 (0.81 to 1.10)	0.47	0.0	0.46
Hemorrhagic stroke†	3	0.75 (0.57 to 0.99)	0.21	36.8	0.04
Ischemic stroke†	4	0.91 (0.82 to 1.01)	0.79	0.0	0.08
Stroke with diabetes†	3	0.80 (0.29 to 2.15)	0.09	58.9	0.65

Dietary Cholesterol restriction is recommended in at-risk population

- Diabetes
  - Diabetes has low apoE and high apo C-III levels (? abnormal CH transport, increase risk of CHD)
  - Insulin sensitivity could influence HDL metabolism and lipoprotein profile (Riemens et al, J Lipid Res 1999; 40:1467).
  - Egg consumption was associated with increased risk of diabetes and mortality in diabetes (Djousse el al, Diabetes Care 2009; 32:295).
- Hyperlipidemic adults

Njike et al. *Nutrition Journal* 2010, **9**:28

RESEARCH Open Access

Daily egg consumption in hyperlipidemic adults - Effects on endothelial function and cardiovascular risk

Randomized controlled trial for 6wk with hyperlipidemic adults (mean age 60 y, TC 244mg/dl)

; Egg consumption has no adverse effect on endothelial function and serum lipids, while egg substitute consumption was beneficial.

Variable	Egg ($n = 36$)	Egg Substitute ($n = 36$)	P Value[2]
Endothelial function			
Flow-mediated dilation, %			
Baseline	5.6 ± 3.9	5.8 ± 3.9	0.78
6 wk	5.3 ± 4.1	6.9 ± 4.0	
Change	−0.1 ± 1.5 ($P = 0.80$)	1.0 ± 1.2 ($P < 0.01$)	<0.01
Adjusted change[3]	−0.2 ± 1.3 ($P = 0.35$)	0.9 ± 1.4 ($P < 0.01$)	<0.01
Total cholesterol, mg/dL			
Baseline	244 ± 24	244 ± 24	1.00
6 wk	239 ± 27	227 ± 27	
Change	−5 ± 21 ($P = 0.10$)	−18 ± 18 ($P < 0.01$)	<0.01
LDL mg/dL			
Baseline	168 ± 17	168 ± 17	
6 wk	165 ± 24	154 ± 24	
Change	−2 ± 19 ($P = 0.30$)	−14 ± 20 ($P < 0.01$)	0.01
HDL, mg/dL			
Baseline	52 ± 15	52 ± 15	1.00
6 wk	51 ± 14	50 ± 13	
Change	−1 ± 11 ($P = 0.53$)	−2 ± 10 ($P = 0.03$)	0.63
Triglycerides, mg/dL			
Baseline	132 ± 52	132 ± 52	
6 wk	118 ± 47	116 ± 50	1.00
Change	−14 ± 37 ($P = 0.54$)	−18 ± 43 ($P = 0.03$)	0.83
Total cholesterol to HDL cholesterol ratio			
Baseline	5.0 ± 1.3	5.0 ± 1.3	1.00
6 wk	5.0 ± 1.2	4.8 ± 1.3	
Change	−0.06 ± 0.66 ($P = 0.54$)	−0.21 ± 0.82 ($P = 0.11$)	0.38

Possible adverse effect of dietary cholesterol

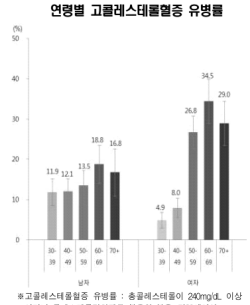
- Dietary CH
  - increases the susceptibility of LDL to oxidation
  - increases postprandial lipemia
  - potentiates the adverse effects of dietary saturated fat (Spence et al. Can J Cardiol 2010; 9:e336)
- Dietary CH worsens macrophage accumulation in adipose tissue, thus increases systemic inflammation and atheroscleosis (Subramanian, Curr Opin Lipidol 2009;20:39)

Trend of blood lipid levels in Koreans

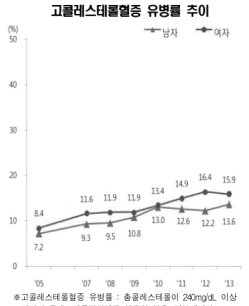
만 19세 이상 (단위: mg/dL)

구분		n	평균	표준오차	백분위수 5	10	25	50	75	90	95
총콜레스테롤											
남자	2005	2,279	183.3	(0.9)	131	142	159	181	205	227	242
	2007~2009	6,836	185.4	(0.6)	133	143	161	183	207	232	246
	2010~2012	7,296	187.7	(0.6)	133	143	163	186	210	233	249
여자	2005	3,096	182.7	(0.8)	133	142	158	179	204	228	242
	2007~2009	9,254	186.7	(0.5)	135	144	161	183	208	234	251
	2010~2012	9,765	188.6	(0.5)	136	145	163	185	210	236	254
LDL 콜레스테롤											
남자	2007~2009	6,596	111.0	(0.5)	63.6	74.0	89.8	109.5	130.3	150.8	163.3
	2010~2012	7,056	112.2	(0.5)	63.0	73.0	90.0	110.7	132.2	152.9	165.6
여자	2007~2009	9,155	113.8	(0.4)	68.6	77.0	91.4	110.6	132.7	155.3	169.6
	2010~2012	9,680	114.5	(0.4)	68.3	77.1	92.1	111.6	133.7	156.0	170.4
HDL 콜레스테롤											
남자	2007~2009	6,836	45.5	(0.2)	32.1	33.9	38.2	44.3	51.3	59.1	63.8
	2010~2012	7,296	46.5	(0.2)	32.1	34.7	39.1	45.2	52.2	60.1	65.2
여자	2007~2009	9,254	50.7	(0.2)	34.7	37.3	42.8	49.5	57.4	65.2	70.5
	2010~2012	9,765	51.9	(0.2)	35.4	38.2	43.9	51.3	58.3	67.0	72.2

Prevalence of hypercholesterolemia in Koreans



※고콜레스테롤혈증 유병률 : 총콜레스테롤이 240mg/dL 이상 이거나 콜레스테롤강하제를 복용한 분율, 만30세이상



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※2005년 추계인구로 연령표준화

Status of cholesterol intake in Koreans

연령 (세)	N	평균 섭취 량 (mg/일)	콜레스테롤 섭취량의 분위수(mg/일)									목표량 초과 섭취자 (%)
			2.5 %	5 %	10 %	25 %	50 %	75 %	90 %	95 %	97.5%	
남자												
19-29	653	420.6	23.0	51.9	82.9	166.8	315.6	563.0	862.5	1134.3	1355.1	53.0
30-49	2160	372.9	19.1	39.0	68.4	150.3	300.1	506.1	757.4	926.4	1122.7	49.9
19-49	2813	387.3	21.4	41.0	73.2	154.7	307.1	522.1	787.4	964.2	1227.1	50.6
50-64	1172	280.0	2.1	11.6	33.8	87.3	197.5	380.5	609.5	856.7	999.0	33.5
65-74	532	200.2	0.0	0.0	3.8	31.4	112.8	278.7	472.7	657.7	871.1	22.7
75+	259	192.3	0.0	0.0	0.3	18.8	66.9	225.2	486.0	711.7	1042.2	17.4
여자												
19-29	877	292.2	16.3	29.3	47.3	107.9	227.5	387.3	624.9	776.8	918.0	38.1
30-49	2804	252.0	8.9	21.9	37.3	87.8	186.4	348.4	541.5	701.9	842.6	32.3
19-49	3681	264.0	10.2	23.8	39.6	91.7	200.1	361.5	562.2	720.4	883.9	33.7
50-64	1152	185.0	0.0	4.0	12.9	43.2	112.7	250.8	438.1	603.2	785.7	19.1
65-74	355	109.2	0.0	0.0	0.0	9.9	45.3	111.9	301.6	418.5	681.6	9.3
75+	336	111.1	0.0	0.0	0.0	9.4	31.6	126.5	277.8	552.4	748.8	8.6

KNHANES 2008-2012

Dietary recommendations for cholesterol

ESC/EAS	<300 mg/d
Dietary Guidelines for Americans(2010)	<300 mg/d(<200mg/d can help for high risk of CVD
Dietary Guidelines Advisory Committee(2015)	No recommendation
National Cholesterol Education Program (NCEP)	
ATP II (1994)	Step1; <300mg/d, step2; <200mg/d
ATP III (2002)	<200 mg/d
AHA/ACC	
guidelines (2006)	<300 mg/d
guideline (2013)	No recommendation
Korea	
Dietary Guidelines for Koreans (2010)	< 300 mg/d
이상지질혈증 치료지침 (2015)	< 300 mg/d
Dietary Guidelines for Koreans (2015)	< 300mg/d

Conclusion

- Dietary CH has only a modest contribution to plasma LDL cholesterol.
- There is insufficient evidence to determine whether lowering dietary CH reduces CHD risk.
- Individual variability in response to dietary CH
  ; No simple way to screen hyper-responders to dietary CH
- Changes in dietary habit and dietary pattern
  ; concern for increasing intakes of fat, saturated fatty acids, trans fatty acids, and cholesterol

? It is prudent to assume the worst when information about risk is uncertain.?