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J. KOREAN SOC. FOOD NUTR.
15(3) 306~312 (1986)

Eggs and Cholesterol Controversy

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Abstract

Demonstration of the highly positive correlation between blood cholestrol levels and heart disease has made consumers wary of the fats in meat, milk and eggs. The egg, as perhaps the single largest common source of cholesterol, has been cited by many members of the medical and scientific world as a food contributing to heart disease.

In light of decreasing per capita egg consumption and continuing dietary egg cholesterol controversy, many researchers have focused their efforts on egg nutrition. The results reported, however, are often contradictory. In spite of the disputable scientific evidence, the egg has been labelled (erroneously) as a highly cholesterogenic food.

The objective of this presentation is to present a general picture of the problem and discuss our laboratory findings relevant to the problem.

An isotope technique was utilized to incorporate ^{14}C-cholesterol into egg yolk lipoproteins and study the metabolic fate of dietary ovo-cholesterol in rats. Two hundred and fifty micro-curies of 4-^{14}C-cholesterol, emulsified in corn oil, were orally administered to five Single Comb White Leghorn laying hens. Eggs were collected, hard-boiled, and the hot dried egg yolk powder (HEY) was prepared.

Total radioactivity excreted via feces was determined. The rat groups fed egg yolk powder excreted more than 95% of the ingested ovo-cholesterol, whereas the rat chow group excreted only 47%. No difference was observed between HEY and CEY treatments. Therefore, an unknown lipid factor present in egg yolk accelerates cholesterol turnover rate and excretion via feces.

Cholestrol controversy

Cholesterol is a complex fatty substance found in the body structure of all animals including humans. It is an essential part of the structure of cell membranes in the body. cholesterol is also the starting material from which the body makes its own supply of sex and adrenal hormones. The body can also convert cholesterol to vitamin D which is essential for calcium metabolism. Hence, the body requires cholesterol, and in fact certain lower forms of animal require cholesterol supply in their diets as an essential nutrient because they have no ability to produce their own requirement. It is clear, therefore that animals and humans alike must have some cholesterol for maintenance of life and normal functions.

Usually, we hear, however, about what is bad for us about cancer causing agents, heart

Key Word: Cholesterol Atherogenesis, Eggs ^{14}C-ovocholesterol, Excretion, Regression.

disease, obesity or sometimes all of these. That may be one reason why research on cholesterol has captured the medical and popular imagination. It traces back to the feeding of cholesterol to rabbits exactly 75 years ago and the extrapolation of the results to humans. There has been a flood of contradictory research on the cholesterol.

The common view of cholesterol is the pathogenesis of atherosclerosis due to high cholesterol in the diet which increases blood levels and leads to deposits in the coronary arteries. It seems oversimplified and somewhat misleading, but it has been widely accepted in the scientific community and by laymen for years.

The highest death rate is due to artery-heart disease among all causes of death particularly in North America. Therefore, epidemiological demonstration of a highly positive correlation between blood cholesterol levels and heart disease has forced the scientific community to spend millions of dollars for cholesterol research.

It has been known for many years that a wide variety of experimental animals can be employed to produce experimental atherosclerosis by feeding cholesterol. The amounts of cholesterol required to induce the disease, however, are usually 15 to 30 times the amounts found in the average human diet. Such experimentation results in extremely high blood cholesterol levels and deposits of lipids in the walls of the blood vessels. The effect of these lipid deposits is to reduce blood flow and weaken the wall of the blood vessel with the eventual result that in fact, a stroke or an aneurysm take place. Many clinical studies have shown a statistical association between higher concentrations of cardiovascular disease. On these bases, a sharp restriction of dietary cholesterol has been recommended. The average cholesterol content of a medium egg is 250 to 300*mg* and a low cholesterol diet has been defined as one containing less than 300*mg* of cholesterol per day per person. This has resulted in restricted egg usage in many diets including those for senior citizens who need a highly digestible form of protein.

Cholesterol in egg yolk

Eggs are probably the most nutritious food item presently available for human consumption. The biological value of other food has often been determined by using eggs as a reference standard. It is probably the only food item in the animal kingdom which supports growth alone and leads to the formation of new life. However, one of the major nutritional problems related to egg consumption is the presence of a high level of cholesterol. The current unsettled status of the relationship between dietary cholesterol and heart disease has an impact on egg consumption by the human population at large. There has been a general recommendation both from laymen and physicians that the dietary cholesterol be restricted as far as possible. In fact, it has been recommended to Canadians that they should "eat no more than four than four eggs per week per person including eggs used in cooking" (5).

Inlight of decreaing per capita consumption and continuing dietary controversy, considerable efforts have been made to reduce the amount of cholesterol in the egg by nutritional and genetic means. It has been known for many years that the degree of unsaturation in egg yolk lipid can be changed by dietary means, but has been only recently shown that cholesterol can be reduced by dietary manipulation.

A number of lipid factors and drugs have been tested for their ability to reduce cholesterol level in blood and egg by feeding or treating laying hens. It is, however, clear that the hypocholesterolemic activity of a drug or dietary agent is not necessarily related to a

reduction in egg yolk cholesterol (9). Feeding plant sterols have been widely studied as a potential dietary manipulation in reduction of egg cholesterol levels by as much as 35 percent (2, 11, 13). The reduction of cholesterol level is merely of statistical significance. No drugs or dietary agents have proved to produce a cholesterol-free or low-cholesterol egg (14).

Dietary ovo-cholesterol and its metabolic fate

In view of the relatively high cholesterol content, egg yolk has been implicated as having extra cholesterogenic properties (8). Eggs have been frequently used as dietary cholesterol sources to induce hypercholesterolemia and atherosclerosis developments in rabbits (1). A search of current literatures, however, indicates minimal or even no changes in human serum cholesterol at different levels of egg in the diet (4, 7). Many investigators have focused their efforts on human subjects to induce hypercholesterolemia by feeding eggs with their normal meal. However, only limited information is available in the recent literature on an animal model testing the cholesterogenic property of egg yolk cholesterol in a direct comparison with equal amounts of the crystalline form.

In our laboratory, a comparative study on the cholesterolemic property of two dietary sources of cholesterol, egg yolk powder vs. the crystalline from, was conducted by feeding two different age groups of chickens (12). The correlation coefficient between dietary and serum cholesterol levels were $r=0.97$ ane 0.77 for the crystalline and egg yolk powder respectively (Fig. 1). Crystalline cholesterol in the diet produces significantly higher serum cholesterol than that of egg yolk powder at the same level.

These results indicate that egg yolk cholesterol is either not available or depresses the serum cholesterol elevation after consumption.

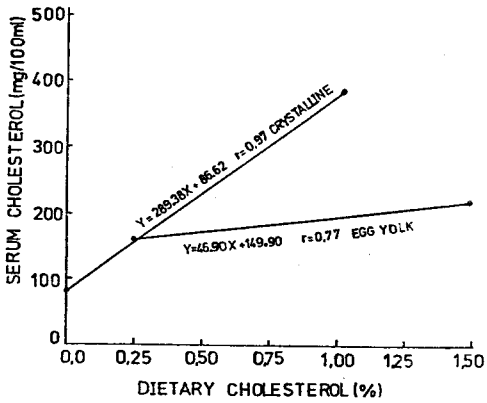

Fig. 1. Regression line of serum cholesterol levels plotted against dietary cholesterol levels of the crystalline form and egg yolk form. The difference between the slopes is highly significant($p<0.01$).

The concept remains valid that serum cholesterol levels depend primarily on the physical-chemical nature of fats which are co-administered (3, 5). The ability to absorb dietary cholesterol is highly dependent upon the nature of dietary lipids co-administered, other than cholesterol itself.

Ovo-cholesterol exists as an integral part of the lipoprotein structure in the low-density particles and lipoproteins of egg yolk (6). The egg yolk lipids are firmly associated with the protein. Thus, the dietary ovo-cholesterol is expected to act differently from the free from of cholesterol in the matabolic system. Therefore, we have examined the metabolic fate of dietary ovo-cholesterol by developing an isotope technique which will permit one to draw definite conclusions regarding the fate of ingested egg yolk cholesterol.

By force-feeding ^{14}C-cholesterol to actively laying birds, radio-active cholesterol was incorporated into egg yolk lipoproteins(Fig. 2). The ^{14}C-cholesterol egg powder (HEY) was fed to a group of adult rats (13). They were paired with a control rat group fed equal amounts of ^{14}C-cholesterol added to cold egg yolk powder

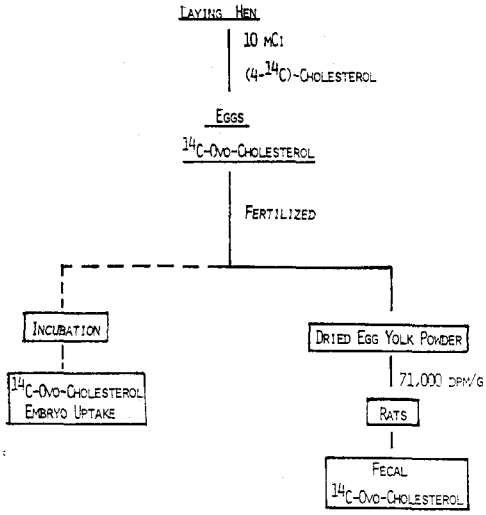

Fig. 2. Flow Sheet For Ovo-Cholesterol Study.

(CEY). Rat Chow (#5012, Ralston Purina Co.) was ground and used as a control (C). Total radio activity excreted via feces was deter mined. The fecal excretion rates of ^{14}C-cholesterol were 92.7 and 98.1% for CEY and HEY diets respectively. In contrast, the rat group fed rat chow control (C) diet excreted only 47 % which is significantly lower ($P<0.01$) than those fed egg yolk powder (Table 1). No significant difference, however, was observed between the CEY and HEY-fed groups. This indicates that the accelerated fecal cholesterol excretion is due to the presence of dietary egg yolk and not necessarily attributed to the physico-chemical structure of intact ovo-cholesterol in the egg yolk lipoproteins. Therefore, results clearly ruled out a possibility that the biomolecular structure of ovocholesterol in the egg yolk lipoproteins is a contributing factor, because simple addition of ^{14}C-cholesterol to the egg yolk diet was as effective as the biologically enriched ^{14}C-ovo-cholesterol in the fecal cholesterol excretion. These results imply that egg yolk contains a factor (s) responsible for accelerated cholesterol metabolism and excretion of the egg yolk-fed rats. The published work to date, however, fails to provide an explanation for the exact role of the dietary egg yolk complex on cholesterol metabolism.

Table 1. The Metabolic Fate of ^{14}C-ovocholesterol in the Egg Yolk Fed Rat (Trial 2.)

	Experimental Diets[1]		
	C[2]	CEY	HEY
Feed Intake (*g*)	40.5±1.4	36.6±0.5	38.0±2.0
Total Feces (*g*)	8.9±0.1	6.2±1.1	5.6±0.4
Dry Matter Digest. (%)	78.1±0.5	83.0±3.2	85.2±0.4
Eecal Recovery of ^{14}C (%)[3]	47.3±3.2(a)	93.7±4.2(b)	98.1±1.9(b)
Sp. Activity (DPM/*mg* cholesterol)			
Cholesterol Fed	77,057.9	6,542.6	7,624.3
Cholesterol Excreted	18,768.2	5,942.7	7,463.5
Ratio	4.1 : 1.0	1.0 : 1.0	1.1 : 0
Plasma ^{14}C (DPM/100*mℓ*)	157,216.6	—	—
Total Plasma Cholesterol Level (*mg*/100*mℓ*)	65.0±1.0	60.0±0.7	59.0±1.3

[1] Values are expressed as Mean±S.E. of three rats.
[2] C (control diet as 100% rat chow), CEY (mixture of equal amount of cold egg yolk powder with rat chow) and HEY (mixture of equal amount of hot egg yolk with rat chow).
[3] Means within a row followed by the same superscrcipt are not significantly different at 1% level of probability.

Earlier research demonstrated acceleration of the bile cholesterol output and a rapid disappearance of tissue cholesterol when egg yolk powder was fed (10, 16). Lecithin, one of the rich components in egg yolk has been suggested as the responsible factor.

Results of this study present a number of questions related to the alleged atherogenic property of eggs in the human. It may also be the reason that many investigators have failed to increase the plasma cholesterol level in man by including eggs in the normal meal.

The exact biochemical role or mechanism of dietary egg yolk accelerating turnover rate of dietary cholesterol cannot be sufficienctly elucidated with the present experimental observations, however, a hypothesis is suggested that egg yolk provides a certain physico-chemical milieu active at the post-absorptive site that enhances cholesterol turnover causing removal from blood.

Dietary egg yolk and regress of atherosclerosis

There is evidence that atherosclerosis lesions in man may regress. Leary (17) has stated that atheromatose lesions need not advance and, indeed, may regress, after the disappearance of cholesterol from the lesions. Horlick and Katz (18) demonstrated regression of atherosclerosis in cholesterol-fed chicks. Within three weeks after cessation of feeding cholesterol, little or no gross evidence of atherosclerosis remained in the aorta, a finding that suggested a complete remission. Reversibility of cholesterol-induced aortic lesions seems related to the total amount of cholesterol ingested and to the duration of the cholesterol feeding (18).

Recent research interest in this laboratory has been concerned with the the possible effect of dietary egg yolk on the regression process of the advanced stage of atherosclerostic lesions. Male cockerels are prone to develope spontaneous atherosclerosis with a high degree of lesion severity without dietary insult when they are older than 12 months of age. A group of adult cockerels selected from a large breeding rooster population which developed spontaneously advanced stage of arterial lesions were employed (Fig. 3).

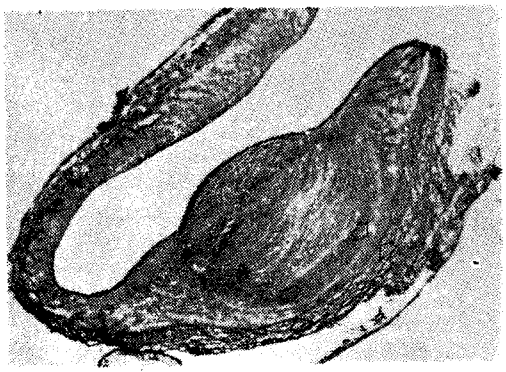

Fig. 3. Naturally occurring atherosclerosis of the abdominal aorta of mature White Leghorn cockerels fed cholesterol-free control diet. Note: focal fibrous intimal plaque adjacent to the very narrowed media (arrows) Hematoxylin-eosin×110.

These studies included a group of cockerels fed an atherogenic diet containing 1.0% of either cystalline cholesterol dissolved in animal fats or egg yolk powder with an equal amount of cholesterol. A cholesterol-free group was the control. After nine weeks on these diets, 12 birds from each treatment group were sacrificed at random to determine the severity of atherosclerosis according to the procedures of Katz and Stamler (18). The aortae were rapidly removed, trimmed of extraneous tissue, opened longitudinally, and grossly graded.

The progression and regression of atherosclerostic lesions in the aorta was assessed by the score system ranging 0 to 4 for the degree of severity. Results revealed that feeding egg yolk powder diminished or halted the developing atherosclerostic lesions from the score of

3.1 to 2.4, while the atherogenic diet containing crystalline cholesterol worsened from 3.1 to 3.62 (Fig. 4). We were quite amazed because such results were not expected on the basis of information present in the literature. This observation brings up two important questions. Spontaneous atherosclerosis lesions developed in the aged cockerels may serve as a best model to human condition and may answer the question: Is aged atherosclerosis lesion reversible?

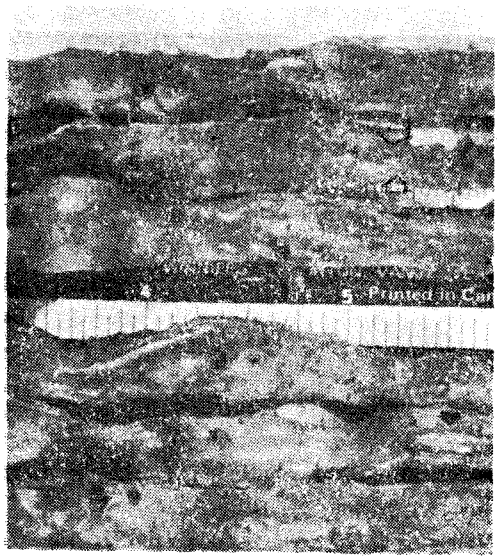

Fig. 4. A view of opened aortae disected from birds fed 1% crystalline from of cholesterol (left) and egg yolk powder from of cholesterol (right). Degree of severity in vascular sclerosis and typical lipid plaques in the area of thoracic and abdominal aortae is found comparable. Diminished fatty streak (open arrow) is comparable with the fatty plaque at the abdominal arteries with crystalline cholesterol treatment (solid arrows).

There is clearly a good deal of confusion about the question of reversibility of advance arterial lesions. The second aspect of questions is whether oral administration of egg yolk is atherogenic or anti-atherogenic to human. It is important indeed to determine whether the reversiblity action of dietary egg yolk is species specific or age related.

An earlier study with rats demonstrated a rapid disappearance of tissue cholesterol when egg yolk powder was fed (10). These workers suggested that the lecithin-rich egg lipids are the reponsible factor. Cholesterol removal rate has been found to vary directly with the bile acid secretion rate and more recently it was proposed that bile acid synthesis rate is determining factor on the rate of cholesterol secretion into bile (19, 20, 21).

Although the published work to date fails to provide an exact explanation for the role of dietary egg yolk complex on cholesterol meta bolism and atherogenesis, results of this study present a number of questions related to the alleged atherogenic property of eggs in the human (8). It may also be the reason why many investigations have failed to increase the plasma cholesterol level in man by including eggs in the normal meal (22, 23, 24, 25). Further work is in dire need.

References

1. Anitschkow, N. Experimental Atherosclerosis in Animals: Review of problem edited by E.V. Coudry, MacMillan, New York, pp. 271, 1933.
2. Clarenburg, R., I.A. Kim Chung and L.M. Wakefield, 1971. Reducing the egg cholesterol level by including emulsified sitosterol in standard chicken diet. *J. Nutr.* ***101***: 289.
3. Holt, P.R. 1972. The role of bile acids during the process of normal fat and cholesterol absorption. *Arch. Intern. Med.* ***130***: 574.
4. Keys, A., J.T. Anderson, O. Adelson and F. Fidanza, 1956. Diet and Serum cholesterol in man: Lack of effect of dietary

cholesterol. *J. Nutr.* **59**: 39.

5. Lewis, B., A. Chait, A.W. Febrary and M. Mattock, 1973. Functional overlap between chylomicra and very low density lipoproteins of human plasma during alimentary lipaemia. *Atherosclerosis* **17**: 455.
6. Martin, W.G., N.H. Tattrie and W.H. Gook, 1963. Lipid extraction and distribution studies of egg yolk lipoproteins. *Can. J. Biochem. Physiol.* **41**: 657.
7. Mayer, G.A., W.F. Connell, M.S. DeWolfe and J.M.R. Beveridge, 1954. Diet and plasma cholesterol levels. *Am. J. Clin. Natr.* **2**: 316.
8. Messinger, W.J., Y. Porosowska and J.M. Steele, 1950. Effect of feeding egg yolk and cholesterol on cholesterol level. *Arch. Int. Med.* **85**: 189.
9. Naber, E.C. 1976. The cholesterol problem, the egg and lipid metabolism in the laying hen. *Poultry Science* **55**: 14.
10. Okey, R. and E.D. Yokela, 1936. The effect of feeding egg yolk on the liver lipids of young rats. *J. Nutr.* **11**: 463.
11. Sim, J.S. and D.B. Bragg, 1977. Effect of dietary factors on serum and egg yolk cholesterol levels of laying hens. *Poultry Science* **56**: 1616.
12. Sim, J.S. W.D. Kitts and D.B. Bragg, 1980. Effect of dietary egg yolk on serum cholesterol levels of White Leghorn Cockerels. *Poultry Science* **59**: 1812.
13. Sim, J.S., W.D. Kitts and D.B. Bragg, 1980. Metabolic fate of C-Ovocholesterol in the egg yolk-fed rat. *Poultry Science* **59**: 1662.
14. Sim, J.s., W.D. Kitts and D.B. Bragg, 1984. Effect of dietary saponin on egg cholesterol level and laying hen performance. *Can. J. Anim. Sci.* **64**: 977.
15. Report of the Committee on Diet and Cardiovascular Disease. Health and Welfare, Canada 1977.
16. Wright, A. and G.H. Whipple, 1934. Bile cholesterol; fluctations due to diet factors, bile sait, liver injury and hemolysis. *J. Expl. Med.* **59**: 411.
17. Leary T. 1944. Cholesterolysis in atheroma. *Arch. Path.* **37**: 16.
18. Katz, L.N. and J. Stamler, 1953. Experimental atherosclerosis. Charles C. Thomas, Springfield, Illinois.
19. Wheeler, H.O. aad K.K. King, 1972. Biliary Excretion of Lecithin and Cholesterol in the Dog. *J. Clin. Invest.* **51**: 1337.
20. Hardison, G.M., and J.T. Apter, 1972. Micellar Theory of Biliary Cholesterol Excretion. *Am. J. Physiol.* **22**: 61~67.
21. Strasberg, S.M. and R.G. Ilson, 1975. Bile Acid Synthesis Rate (BSy), a Determinant of Cholesterol Secretion Rate (CSR). *Gastroenterology* **69**: 869.
22. Porter, M.W., W. Yamanaka, S.D. Carlson and M.A. Flynn, 1977. Effect of Dietary Egg on Serum Cholesterol and Triglyceride of Human Males. *Am. J. Clin. Nutr.* **30**: 490.
23. Slater, G., J. Mead, G. Dhopeshworkar, S. Robinson and R.B. Alfin-Slater, 1976. Plasma Cholesterol and Triglycerides in Men with Added Egges in the Diet. Nutr. *Report International* **142**: 249.
24. Morris, M.L., V.M. Fuller, V.M. Bruce and B.E. MacDonald, 1977. Absorption of Cholesterol from Eggs and the Effect on Serum Cholesterol Levels of Men. *J. Can. Diet Assoc.* **38**(1): 58.
25. Keys, A., J.T. Anderson, O. Adelson and F. Fidanza, 1956. Diet and Serum Cholesterol in Man: Lack of Effect of Dietary Cholesterol. *J. Nutr.* **59**: 39.