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closeUP

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INSIDE

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Nutrition Close-Up is a quarterly publication of the American Egg Board, written and produced by the Egg Nutrition Center. *Nutrition Close-Up* presents up-to-date reviews, summaries and commentaries on the latest research on the role of diet in health promotion and disease prevention, including the contributions of eggs to a nutritious and healthful diet. Nutrition and health care professionals can receive a **free** subscription for the newsletter by contacting the Egg Nutrition Center.

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Obesity, Insulin Resistance, and Heart Disease

The cluster of risk factors characteristic of the metabolic syndrome— hypertension, dyslipidemia, central obesity, and insulin-resistance—have become all-too-familiar signs of our time. It should come as no surprise that an estimated 20-25% of US adults have metabolic syndrome, which means an increase in the risk of heart disease for nearly a quarter of the US population. The link between insulin-resistance, obesity, and heart disease risk has been well established, but whether these conditions are related to altered effects of dietary lipids on cholesterol metabolism is still unknown. Although dietary interventions to reduce risk in obese, insulin-resistant individuals are clearly needed, research investigating responses to increased dietary fat and cholesterol in this population is limited.

Researchers at the University of Washington undertook an egg feeding study to determine the influence of dietary fat and cholesterol on the lipid profiles of obese and non-obese individuals with varying degrees of insulin sensitivity. After potential participants were excluded based on elevated total cholesterol (>300 mg/dL), and TAG (>500 mg/dL) levels, blood pressure, presence of diabetes, anemia, coronary or peripheral vascular insufficiency, renal, liver, or uncontrolled thyroid disease, 220 individuals were enrolled to participate in this study.

Participants were categorized as obese (based on BMI $\geq$ 27.5 kg/m^2) or non-obese and insulin-sensitive or insulin-

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Obesity, cont...

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resistant (based on insulin-sensitivity index score), after which they were randomly assigned to one of three treatment groups: 0 yolks/day, 2 yolks/day, or 4 yolks/day. Vital signs, height, weight, waist to hip ratio, fasting glucose, blood lipid levels, and apoprotein (apo) B were measured at baseline. Each treatment period was 30 days in duration and was followed by a 30-day washout period. By the end of the three treatment periods, there were 197 participants remaining. Vital signs, serum lipoprotein levels, and diet histories (using 3-day food records) were obtained before and after each intervention period.

Of the 197 participants, 65 were classified as insulin-sensitive (IS), 75 as insulin-resistant (IR), and 57 as obese and insulin-resistant (OIR). Because they were so few in number, the 12 participants who were classified as IS and obese were excluded from the study. As expected, IS participants were younger and reported more frequent aerobic exercise than IR or OIR participants. At baseline, body weight, blood pressure, and intra-abdominal, subcutaneous and total body fat were incrementally higher across groups (lowest in IS participants, highest in OIR participants).

Participants were asked to consume a diet consistent with the National Cholesterol Education Program (NCEP) Step I guidelines for total fat and saturated fat intake (<30% calories from fat and <10% calories from SFA) for the duration of the study and received periodic dietary counseling.

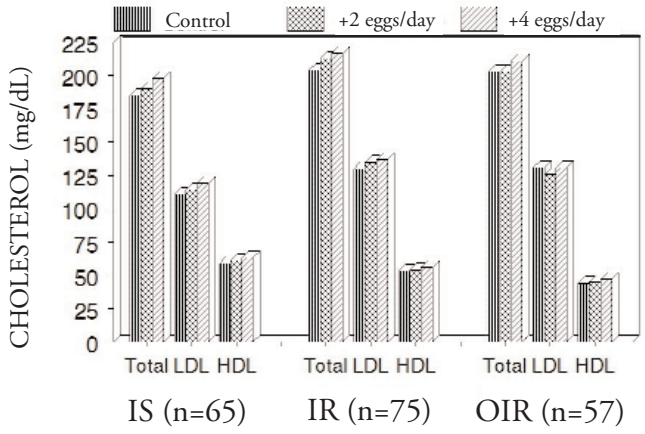
Although compliance with intervention and control diets was good for all groups, the IS participants consumed significantly less SFA than their IR and OIR counterparts. Reported cholesterol intakes for the three groups were 186, 192, and 258 mg/day, respectively.

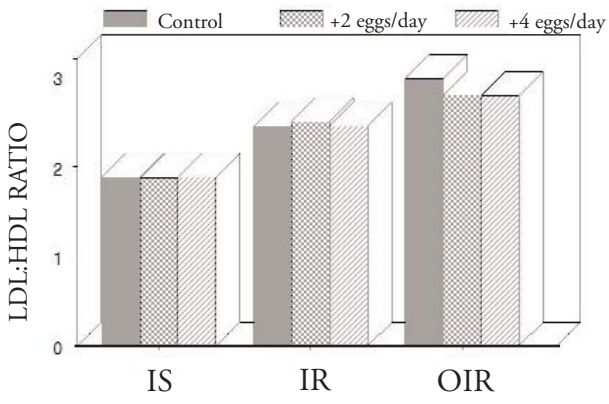
The 108 g egg placebo was comprised of 45 calories, 0 g fat, and 0 mg cholesterol. The two egg preparation contained 34 g egg yolk, 64 g Egg Beaters®, and 10 g water (171 calories, 10 g fat, 425 mg cholesterol). The 4 egg preparation consisted of 68 g egg yolk, 20 g Egg Beaters®, and 20 g water (298 calories, 20 g fat, and 850 mg cholesterol). A one-month supply of the egg preparation was provided to each participant at the beginning of each intervention. No other food was provided by the investigators. Participants followed the intervention and control diets at home ad lib.

At baseline, total, LDL, and non-HDL plasma cholesterol as well as apo-B levels were higher in IR and OIR participants than in IS participants. Plasma TAG levels were 91, 119, and 159 mg/dL for IS, IR, and OIR groups, respectively. HDL cholesterol levels and LDL buoyancy fell across groups, with IS participants having the highest and OIR participants having the lowest HDL cholesterol levels. (More buoyant LDL particles are thought to be less atherogenic.) While plasma total cholesterol increased with the 4-egg/day regimen for all three groups, the greatest increase was observed in the IS participants, who began the study with the lowest baseline LDL cholesterol levels and the lowest dietary cholesterol intake (refer to figure at bottom left). TAG levels were significantly lower in IS participants following the 4-egg/day regimen. These levels did not fall during the 0 or 2-egg/day intervention or in any other group.

Interestingly, although LDL cholesterol levels increased significantly in the IS and IR groups (7.8% and 3.3%, respectively) following egg feeding, no increase occurred in the OIR group, suggesting that cholesterol metabolism is altered in a combined state of obesity and insulin resistance. These results were similar after controlling for baseline differences in LDL cholesterol levels, and for differences in intake of cholesterol, saturated fat, and polyunsaturated fat in the background diet.

Combined data for IS participants following the 2- and 4-egg/day regimens showed an increase in buoyant LDL particles and a decrease in IDL particles. Notably, the increased LDL levels following egg feeding were accompanied by corresponding increases in HDL levels for





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all groups—a result that should not be ignored given the importance of the LDL:HDL ratio in predicting heart disease risk (refer to figure at bottom right, pg 2).

The most significant findings of this study are three-fold. First, insulin-resistant individuals have a tendency toward markedly increased LDL cholesterol levels whether or not obesity is present. TAG levels are also elevated and HDL cholesterol levels are decreased in states of insulin resistance. These differences are more marked in obese insulin-resistant individuals.

Second, insulin-sensitive participants experienced a heightened LDL cholesterol raising response to egg feeding when compared with insulin-resistant subjects. The authors speculate that the blunted rise in LDL cholesterol observed in insulin-resistant participants was due to decreased cholesterol absorption, which has been observed in other studies dealing with insulin resistance.

A third interesting aspect of the LDL cholesterol response to egg feeding in this study is that the only significant rise in LDL levels occurred in insulin-sensitive participants who were consuming 4 eggs daily. This increased LDL level was balanced by a concurrent rise in HDL cholesterol and was comprised mostly of more buoyant, less atherogenic particles.

Because dietary composition appears to have little to do with serum cholesterol responses in insulin-resistant individuals, the authors conclude that diet therapy for these patients should focus on calorie restriction and liberalization of fat content to improve satiety.

Knopp RH, Retzlaff B, Fish B, et al. Effects of insulin resistance and obesity on lipoproteins and sensitivity to egg feeding. *Arterioscler Thromb Vasc Biol.* 2003;23:1437-1443.

Key messages

- Insulin resistance with or without obesity is usually accompanied by increased LDL cholesterol levels. Insulin resistance is also associated with decreased HDL cholesterol levels and elevated TAG concentrations, which are exacerbated in the presence of obesity.
- Insulin-resistant participants experienced a smaller increase in LDL cholesterol in response to egg feeding than those who were insulin-sensitive.
- Insulin-resistant patients might benefit more from diets that focus on calorie reduction and allow a higher fat intake for increased satiety.

Comment

Overweight and obese individuals following high-protein, low-carbohydrate diets for weight control frequently report eating 3-5 eggs daily without an increase in serum cholesterol levels. They are often surprised to find their serum cholesterol levels improved with weight loss, regardless of dietary cholesterol intake.Though anecdotal, the observation appears to be getting some scientific support. The findings of Knopp et al. support those of Reaven and colleagues (*Metabolism.* 2001;50(5):594-597), who found that obese insulin-resistant individuals do not experience significant increases in serum total or LDL cholesterol with increased dietary cholesterol intake. Further, the data presented by Knopp et al. support the findings of Miettinen and colleagues (*Am J Clin Nutr.* 2000;72:82-88; *J Lipid Res.* 2002;43:1472-1476; *Diabetes Care*. 2002;25:1511-1515.) who observed a decrease in the absorption of dietary cholesterol in insulin-resistant individuals. They also found that overweight subjects who lost weight experienced increased cholesterol absorption.

COMMON ABBREVIATIONS

BMI: body mass index (kg/m^2)
CHD: coronary heart disease
CHO: carbohydrate
CVD: cardiovascular disease
HDL: high density lipoprotein
LDL: low density lipoprotein
Lp(a): lipoprotein (a)
MUFA: monounsaturated fatty acids
PUFA: polyunsaturated fatty acids
PVD: peripheral vascular disease
RR: relative risk
SFA: saturated fatty acids
TAG: triacylglycerol
VLDL: very low density lipoprotein

Editorial: *In Science, Perception is Not Reality*

An open letter to Center for Science in the Public Interest Director, Michael Jacobsen

The mixing of science, politics, agendas, and self-aggrandizing—when used to harm individuals who don't happen to endorse your opinions—is a sad commentary on CSPI. Your media event criticizing the USDA-HHS Dietary Guidelines Advisory Committee is another example of the intolerant attitude and irrational knee-jerk judgementalism expected from CSPI.

Unhappy with 7 of the 13 appointees, CSPI publicly questioned their suitability through character assassination. These top ranked, highly regarded, well published, nationally and internationally recognized leaders fail in your eyes because they had the audacity to accept research grants or advisory panel positions or sponsored lectureships from—or simply talked to members of—the FOOD INDUSTRY! Guilt by association at its worst.

Your concern is not that they fail to be in the top tier of research scientists, educators, mentors, and leaders, but that they are open minded and associate with CORPORATIONS! In your "Oh my God how dare you!" letter to USDA, and comments to the media, you indicated (with the usual lack of wit and charm) that these individuals had substantial funding from the sugar, egg, chocolate, dairy and other food-related industries, and that the chosen experts' "biases" should disqualify them since "Few people, after all, want to bite the hands that feed them."

But you left out a few key points, Mike. Let me tell you what 15 minutes with Google™ and PubMed reveals about these "biased" experts. [And, for the sake of full disclosure, I consider them colleagues and some are friends. And none of them has received "substantial funding" from the egg industry.]

CSPI: "Fergus M. Clydesdale, professor at the University of Massachusetts, has held stock in and consulted for several food-related companies. "

Dr. Clydesdale is Distinguished Professor and Head of the Department of Food Science, University of Massachusetts Amherst, an expert on food policy, author of over 360 scientific articles, and co-authored/co-edited 20 books. He served on the Keystone Committee on National Policy on Diet and Health, Food and Nutrition Board of the National Academy of Sciences, and FDA Food Advisory Committee. He received the Institute of Food Technologists highest honor, and CAST's Charles A. Black Award for scientific communication. [Maybe that's why food companies want to consult with him.]

CSPI: "Vay Liang, professor at the University of California at Los Angeles, has received funding from numerous drug companies."

Vay Liang W. Go, M.D. is Professor of Medicine at the UCLA School of Medicine; Director, UCLA Nutrition Education Program; Associate Director, UCLA Clinical Nutrition Research Unit; Founder & Past President of the American Pancreatic Association; Editor of *Pancreas*; Member of the FDA Advisory Committee on Gastrointestinal Drugs; and Chair of the Research Program Evaluation Committee for the American Institute of Cancer Research. His awards include the Research Achievement Award from the American Institute of Cancer Research and Lifetime Achievement Award from the American Pancreatic Association. He has published 320 original papers and 117 book chapters, reviews and editorials, and co-edited Nutritional Oncology. [And Mike, there are researchers testing effective drug treatments for pancreatic cancer.]

CSPI: "Penny Kris-Etherton, professor at Pennsylvania State University, has consulted for Campbell Soup and Procter & Gamble. "

Penny M. Kris-Etherton, Ph.D., R.D. is Distinguished Professor of Nutrition at Pennsylvania State University. Dr. Kris-Etherton's research focuses on the regulation of lipoprotein metabolism and has generated many significant contributions to understanding how exercise, smoking, weight loss and diet affect blood lipids and cardiovascular health. She has served on the AHA Nutrition Committee and the IOM-NAS Macronutrient Committee. A check of PubMed lists 128 peer reviewed articles dealing with diet and lipids. [And yes, Mike, because she is an expert on diet and lipids, the egg industry has occasionally consulted with Dr. Kris-Etherton, who I've personally known and respected for many years.]

CSPI: "Theresa Nicklas, professor at Baylor College, has conducted research funded by the Sugar Association and the Kellogg Company."

Theresa A. Nicklas, DrPH, LN is Professor of Pediatrics at Baylor College of Medicine with research on factors influencing eating patterns in childhood as related to obesity and type 2 diabetes and intervention strategies for maintaining healthful behavior. Her CSPI judged sin? She had the impudence to say "The majority of the studies available looking at the relationship between obesity and sugar consumption are negative…" And she no doubt said it based on 80 plus publications on diet and health in children. The Bogalusa Heart Study was a gold mine for collecting and analyzing data to test a hypothesis. [You do remember data analysis from your doctoral studies, don't you Mike?]

CSPI: "Russell Pate, professor at the University of South Carolina, has received at least $200,000 from industry-funded International Life Sciences Institute."

Russell R. Pate, Ph.D. is Professor in the Department of Exercise Science at the University of South Carolina, Columbia. He studies physical activity in the prevention of obesity. And that questionable funding from ILSI? A fellowship program to facilitate linkages

between the school and community to promote physical activity in children. Dr. Pate's "substantial" funding comes from NIH/NHLBI, a 6 yr Trial of Activity for Adolescent Girls ($4,075,000) and a 3 yr Promotion of Physical Activity in High School Girls ($1,981,000). [So, Mike, is he going to forfeit credibility with biases for fellowship support versus a few million from NIH? What was that about the "hand that feeds them"?]

CSPI: "Xavier Pi-Sunyer, professor at Columbia University, has been a paid consultant or advisor to numerous drug companies and received research support from Campbell Soup and Warner-Lambert."

Xavier Pi-Sunyer, M.D. is Director of the New York Obesity Research Center at St. Luke's-Roosevelt Hospital. Dr. Pi-Sunyer has served as President of: American Society for Clinical Nutrition, American Diabetes Association, and North American Association for the Study of Obesity; and has served as Chairman of the NHLBI Task Force on the Treatment of Obesity; member of the WHO International Obesity Task Force, and member of the NIDDK Task Force on The Prevention and Treatment of Obesity. He has published over 175 articles on obesity, diabetes, and nutrition, plus authoring 82 book chapters and editing 2 books. [Unfathomable why the food industry would have any interest in what he has to say about nutrition and health.]

CSPI: "Connie M. Weaver, professor at Purdue University, has conducted research for the National Dairy Council, National Dairy Board, and Procter & Gamble."

Connie M. Weaver, Ph.D. is Distinguished Professor and Head of the Department of Foods and Nutrition at Purdue University. She received the Atwater Lecturership award from Agricultural Research Service, USDA and American Society for Nutritional Sciences. She has served as Chair of the Nutrition Study Section NIH, on the Board of Trustees for the ILSI, and an Advisory Council Member for the Joint Institute for Food Safety and Applied Nutrition. Quick peek at PubMed gets 89 papers. Dr. Weaver's research has focused for many years on calcium metabolism [of some interest to the dairy industry].

But Mike, at least be consistent. You failed to note that the CSPI recommended appointee has received research support from Abbott Laboratories, AstraZeneca Pharmaceuticals, Aventis Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc., ClinTrials Research, Dey Laboratories, GlaxoSmithKline, Glaxo Wellcome Inc., Merck Research Laboratories, Monaghan Medical Corp., Schering/Key Pharmaceuticals, Sepracor Inc., and SmithKline Beecham Pharmaceuticals. Now, I have no problem with this—but then again, I don't live on the lofty moral high ground you do.

And what does the scientific community say about these individuals whose objectivity you question? FANSA (Food and Nutrition Science Alliance), with over 100,000 food, nutrition and medical practitioners and scientists, wrote "As their professional stature in the nutrition, scientific, and academic communities attest, their collective expertise and perspective will well serve the public in the formulation of critical dietary advice." But then, what can scientists (who no doubt feed at the corporate trough) know? Clearly we need you to judge credibility and professionalism. But Mike, what is the evidence for these "biases" that should disqualify them? Show us the evidence, Mike!

I will admit that I take your defamation of their credibility and professionalism personally since I've been on both sides of the issue—as a researcher trying to support a program and as a grants administrator trying to get the best research accomplished (even with CSPI-generated investigator concerns about "industry funded" studies). And in the past CSPI has had its go at eggs and at my own reputation and credibility. My conflicts of interest: I've had grants from anyone who'd fund me (meat, milk, eggs, NIH, USDA, AHA, foundations, and family—if they had offered) as long as they honored my professionalism. I served on advisory panels for everything from eggs to avocados. But the studies were mine, the data were mine, the analysis and interpretation of the data were mine, and the writing was mine. No one told me what to think or say or do. I've trained 10 PhD and 3 MS students, published 92 peer-reviewed papers, 26 book chapters, 13 symposium proceedings, and served on a variety of panels and committees. Today I am proud to be funded by the egg industry using science and facts to correct the damage done by you and your paternalistic colleagues who would ban eggs along with almost everything else.

So tell me, Mike, what new knowledge have you generated from original research? Who of the next generation of scientists have your mentored? How many students have you taught? How much service and leadership have you provided to your profession? You try to negate the honor and character of those you don't even know. They are just media fodder for the CSPI donation machine. They are "biased" because they do not fall into lock-step with your dogmatic beliefs, they do not succumb to your media-hyped scare tactics, and they do not suffer fools who unashamedly proclaim, **"CSPI is proud about finding something wrong with practically everything."** (Washingtonian magazine, February 1994). [Reminds me of the TV ad, "Give it to Mikey, he hates everything."] Well, you clearly did the best members of the scientific community a disservice raising bogus concerns and questions with media-hyped charges of bias and conflict of interest directed at those who really are serving their profession and the public. But then again, those of us who take science and truth seriously understand why you do what you do. To paraphrase an old saying "Those who can, do. Those who can't, bitch about those who can."

Donald J. McNamara, Ph.D.
Executive Editor, Nutrition Close-Up

Effects of Increased Egg Consumption on Lipid Profiles

In the late 1950's, Ancel Keys proposed the hypothesis that dietary fat and cholesterol were directly related to the incidence of coronary heart disease (CHD). This theory, now known as the lipid hypothesis, gradually established itself as part of the widely accepted scientific dogma surrounding dietary lipids. Since then, the fear that any cholesterol consumed at the breakfast table would inevitably wind up lodged between intimal layers of the vascular endothelium has become a common belief among health professionals and consumers alike. Fortunately, advances in lipid research over the past several decades have led scientists to recognize the complexities of cholesterol and lipid metabolism. Although, as Keys suggested, intake of dietary fat and cholesterol appears to be related to coronary heart disease incidence in some individuals, researchers are beginning to question the simplicity of the lipid hypothesis and whether its health message can be accurately translated into population-wide diet prescriptions.

The research challenging this direct relationship between cholesterol intake, serum cholesterol levels, and CHD is based on three tenets: 1) that dietary cholesterol does not translate directly into blood cholesterol; its metabolism is mediated by a number of factors, many of which have genetic components; 2) that individuals react differently to dietary cholesterol and appear genetically predisposed to being hypo- or hyper-responders; and 3) that while cholesterol intake can influence plasma cholesterol levels, saturated fat intake is the strongest dietary determinant of serum total and LDL cholesterol concentrations.

Recently, Herron and colleagues undertook a study examining the effects of increased dietary cholesterol on the lipid profiles of men classified as either hypo- or hyper-responders. This research had three objectives 1) to clarify the effect of prolonged intake of dietary cholesterol from eggs on the lipid profiles of healthy men, 2) to examine the mechanism by which hyper-responders deal with increased plasma cholesterol, and 3) to evaluate differences between men and women regarding responses to increased dietary cholesterol (by comparison to a previous, similar study in women).

Forty men, aged 20 to 50, were recruited from the local community for participation in this randomized crossover study. Potential participants were excluded on the basis of existing hyper-cholesterolemia (TC >219 mg/dL), hypertriglyceridemia, hypertension, and diabetes. Patients taking lipid-lowering drugs were also excluded from participation.

Participating men were randomly assigned to either the treatment or control group to initiate the study. Participants in the treatment group were instructed to consume liquid whole eggs equal to 3 eggs per day (providing ~640 mg/day dietary cholesterol). Those in the control group were instructed to consume an equal weight of liquid egg substitute (providing 0 mg/day dietary cholesterol). This initial phase, lasting 30 days, was followed by a 3-week washout period and a crossover phase in which those participants previously assigned to the treatment group followed the placebo regimen for another 30 days, and vice versa.

All participants were instructed to follow the National Cholesterol Education Program (NCEP) Step 1 diet (<30% of total calories from fat, <10% from SFA, and <300 mg dietary cholesterol) throughout the study. (During the egg intervention period, whole eggs were added to this base diet, such that while following the egg regimen participants were consuming 640-940 mg cholesterol per day). Compliance was measured using seven 24-hr dietary records per treatment period. Serum lipid levels, along with apo B, apo E, and apo C-III, were measured at the beginning and end of both treatment periods. To assess the influence of other factors on changes in lipid profiles, weight, blood pressure, physical activity level, smoking, and alcohol consumption were measured at study initiation and following each treatment period for later evaluation.

Both groups were compliant with dietary directives, as determined by 24-hr food records. Plasma levels of TC, LDL, HDL, and TAG were similar for all participants at baseline. Upon analysis of blood lipids, 25 men were classified as hypo-responders and 15 as hyper-responders. Hyper-response was defined as an increase in TC of >2.32 mg/dL for every additional 100 mg of dietary cholesterol, which translates to an increase of 14.8 mg/dL (the expected rise in TC with the addition of 640 mg dietary cholesterol/day) for the purposes of this study.

There were no significant differences between hypo- and hyper-responders with regard to BMI (mean BMI 24.9 kg/m^2 for hypo-responders vs. 26.1 kg/m^2 for hyper-responders), weight, blood pressure, or level of physical activity at the end of the study. For hypo-responders, there were no significant differences in LDL, HDL, TG or the LDL:HDL ratio following the whole egg regimen vs. the control regimen. Differences were observed among hyper-responders in LDL (85.4 vs. 111.0 mg/dL; $P<0.0001$), HDL (46.0 vs. 49.9 mg/dL; $P<0.05$), and the LDL:HDL ratio (1.91 vs. 2.33; $P<0.05$) following the placebo vs. whole egg regimen, respectively, but plasma TAG levels remained unchanged. For hyper-responders, but not for hypo-responders, significant increases were observed in plasma lecithin cholesterol acyl transferase (LCAT) and cholesterol ester

transfer protein (CETP) activities ($P<0.05$) following the whole egg regimen, indicating an upregulation of reverse cholesterol transport in these individuals. There was no rise in plasma apo B concentration to parallel the increase in plasma LDL in hyper-responders. Likewise, there were no significant differences in apo E or C-III levels following either treatment.

Results from a similar study, previously conducted with premenopausal female participants, were used to compare differences between male and female responses to a cholesterol challenge. While no differences were observed in LDL, HDL, or the LDL:HDL ratio among hypo-responders of either gender, significant increases in LDL and HDL levels were seen in hyper-responders of both genders. The LDL:HDL ratio increased following the cholesterol challenge in male, but not female, hyper-responders.

LCAT accelerates the transfer of cholesterol from non-liver cells and lipoproteins to the liver, where it can be eliminated from the body (thus helping keep plasma cholesterol levels in check). This cholesterol transfer is facilitated by CETP. The heightened activity of LCAT and CETP seen in hyper-responders suggests that the process of reverse cholesterol transport (from the peripheral tissues to the liver for elimination in the bile) was accelerated in response to increased dietary cholesterol.

Since each LDL particle is associated with just one apo B, it is interesting to note that there was no increase in apo B concentrations among hyper-responders, whose LDL cholesterol levels increased. The authors speculate that the increased plasma LDL concentration might have been due to an increase in particle size, rather than number. The concept that LDL particles of varying size and density possess more or less atherogenicity is relatively new, however, it is commonly thought that large LDL particles are less atherogenic than their smaller, denser counterparts, which can more easily enter the vascular endothelium and are more susceptible to oxidation. It is important to note that the experimental diet did not result in elevated TAG levels for either hypo- or hyper-responders, nor did it result in increased apo C-III (which is associated with elevated TAG levels).

As this was a short-term feeding study, its results provide no information on whether a prolonged diet of 3 eggs/day would cause LDL cholesterol levels to rise further in hyper-responders or if a leveling-off would occur. Longer feeding trials are necessary to determine long-term responses in different populations. However, the implications of the present study are significant in that they show that the risk for atherosclerosis is not increased for hypo- or hyper-responsive men or women following a considerable increase in cholesterol intake for a 30-day period. The researchers conclude that their results "indicate that premenopausal women and men with initial plasma cholesterol concentrations that place them at a low risk for CHD do not develop an atherogenic lipoprotein profile after the consumption of additional dietary cholesterol, regardless of their response classification."

In summary, this study suggests that 1) in healthy men and women—both hypo- and hyper-responders—with desirable blood cholesterol levels, short-term increases in cholesterol consumption do not result in atherogenic lipid profiles; 2) increased dietary cholesterol results in an up-regulation of reverse cholesterol transport (from peripheral tissues to the liver); 3) Although TC, LDL, and HDL levels increased following the cholesterol challenge for both male and female hyper-responders, the LDL:HDL ratio increased only in male hyperresponders.

Herron KL, Vega-Lopez S, Conde K, et al. Men classified as hypo- or hyperresponders to dietary cholesterol feeding exhibit differences in lipoprotein metabolism. *J Nutr.* 2003;133(4):1036-42.

Carotenoids and Coronary Artery Disease

The potential of dietary carotenoids to scavenge free-radicals in the lipid fraction has made this class of antioxidants a prime subject for coronary artery disease (CAD) prevention research. Carotenoids, such as lutein, lycopene, beta-cryptoxanthin, alpha- and beta-carotene, have been shown to inhibit lipid peroxidation in vitro. Evidence suggests that these plant compounds directly inhibit LDL oxidation, which is thought to be an obligatory step in atherogenesis. Observational research has shown dietary carotenoid intake and serum carotenoid levels to be associated with decreased risk for CAD. Although research indicates a protective effect of beta-carotene, supplementation trials have failed to demonstrate its independent contribution, suggesting that other antioxidants in beta-carotene rich foods might act synergistically.

To assess the influence of dietary carotenoids on the development of CAD in women, researchers examined dietary and clinical data from 73,286 participants in the Nurses' Health Study. Semiquantitative food frequency questionnaires were completed by participants in 1984, 1986, 1990, and 1994. For each food item, participants were asked to note frequency of consumption for the past year. Responses ranged from "never or less than one per month" to "six or more times per day." Women were also asked about multivitamin use and single-vitamin supplement use. For statistical purposes, participants were divided into five groups based on quintiles of carotenoid intake.

Along with dietary information, the investigators collected relevant clinical information such as height, weight,

Carotenoids cont...

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smoking status, menopausal status and postmenopausal hormone use, presence of diabetes, high blood pressure, hypercholesterolemia, parental history of myocardial infarction (MI), aspirin use, and physical activity level for use in multivariate analysis. Women with incomplete diet records or who were diagnosed with cancer or CVD before 1984 were excluded from the analysis.

After 12 years of follow-up (1984-1996), 998 cases of CAD had been reported including 718 nonfatal MIs and 280 fatal coronary events. After adjustment for other CAD risk factors, women in the highest quintile of beta-carotene intake and in the top two quintiles of alpha-carotene intake exhibited modest risk reductions. Risk reductions associated with dietary lutein/zeaxanthin were not significant after adjustment for the factors listed above.

When participants in the lowest and highest quintiles of intake were compared, women with the highest intakes of beta-carotene, alpha-carotene, and lutein/zeaxanthin were 26%, 20%, and 10% less likely to experience CAD events, respectively.

Some researchers have proposed that while increasing beta-carotene consumption might prove beneficial for individuals with already low intakes, those with higher intakes might not see any benefits from increasing consumption. This is one possible explanation for the lack of data supporting the effectiveness of beta-carotene supplementation. Data from the Nurses' Health Study showing that protection against CAD did not increase beyond the third quintile of intake support this hypothesis.

Since consumption of beta-carotene was associated with increased consumption of all other carotenoids, particularly alpha-carotene (r=0.78), it is difficult to infer that the protection associated with beta-carotene was independent of other carotenoids. Risk reductions associated with higher intakes of lutein/zeaxanthin, lycopene, and beta-cryptoxanthin were not significant. It is possible that dietary carotenoids interact with other antioxidants to confer health benefits.

Since the intake of alpha- and beta-carotene along with other carotenoids is associated with additional lifestyle components that are related to a reduced risk for CAD, data from this study should not be interpreted as supporting supplementation with large doses of alpha- or beta-carotene or any other carotenoid. These data do add to the body of evidence that supports increased fruit and vegetable consumption for reducing CAD risk.

Osganian SK, Stampfer MJ, Rimm E, et al. Dietary carotenoids and risk of coronary artery disease in women. *Am J Clin Nutr.* 2003;77:1390-9.

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