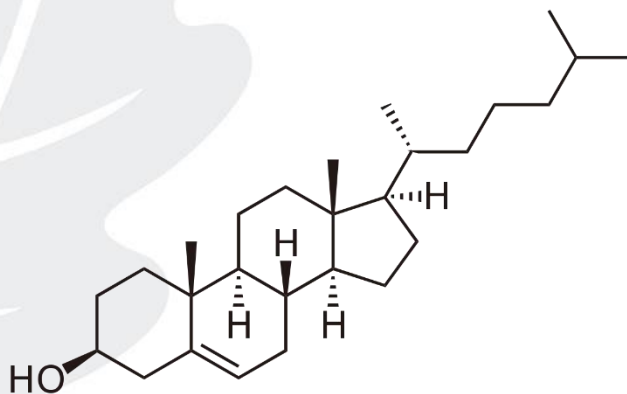


# Dietary cholesterol, serum lipids, and heart disease: are eggs working for or against you?

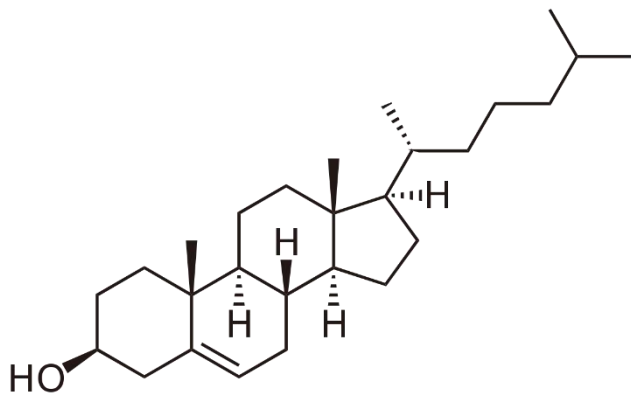


Christopher Blesso, Ph.D.

October 5, 2016

# Overview

- Dietary cholesterol, eggs, and serum cholesterol
- LDL, HDL, and the LDL/HDL ratio in clinical studies
- Lipoprotein particles and heart disease
- Egg sphingomyelin and cholesterol levels

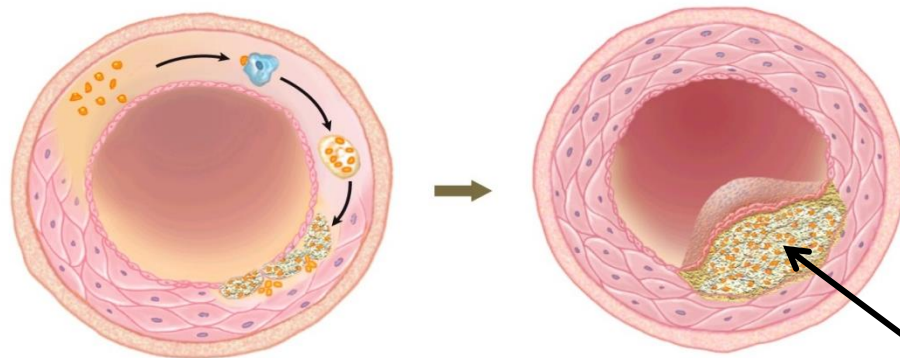


# Cholesterol and heart disease

- **Atherosclerosis** – disease in which cholesterol and fibrous materials are deposited in artery walls, contributes to heart disease
  - **Blockage of blood flow**, death of heart cells (**heart attack**) or brain cells (**stroke**)

Key factors:

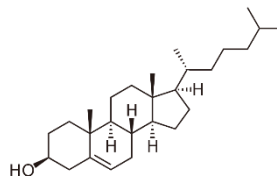
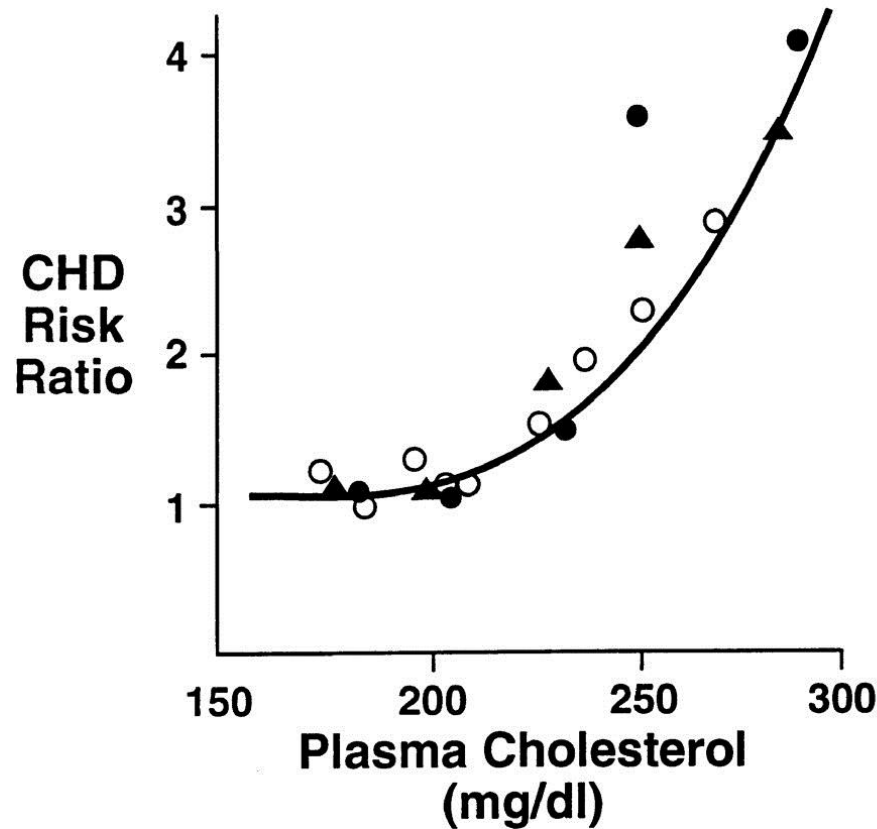
- Serum cholesterol
- Inflammation



Copyright © 2013 John Wiley & Sons, Inc. All rights reserved.

Cholesterol &  
fibrous material

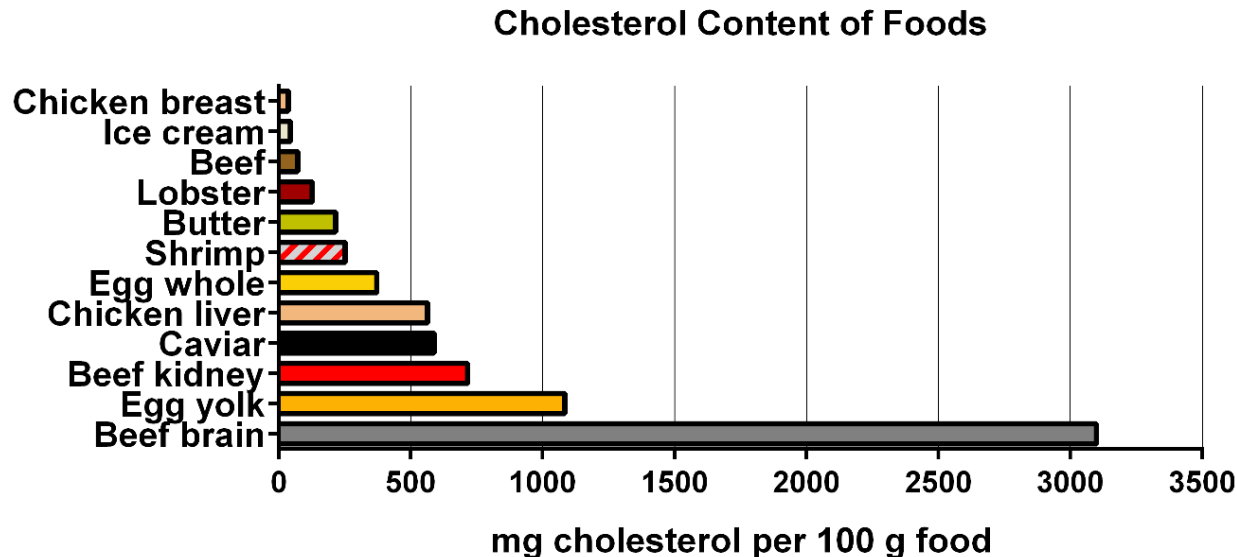
# Relationship between blood cholesterol and risk for coronary heart disease (CHD) in observational studies



# Egg yolk and dietary cholesterol



- **1 large egg yolk contains 185-200 mg cholesterol**
  - Relatively low in saturated fat (19% kcal from saturated fat)
- Average daily intake in U.S. is 270 mg/day
- ***25% of total cholesterol intake in U.S. comes from egg products***





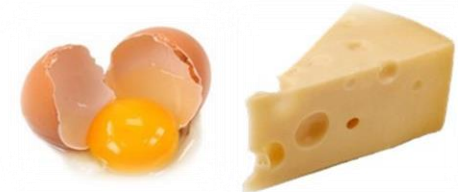
# Is egg consumption linked with heart disease in observational studies?



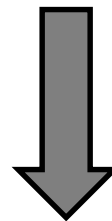
- **Healthy populations:** Most studies show a lack of association between egg consumption and heart disease<sup>1,2</sup>
- **Diabetics:** Meta-analyses show 54%<sup>1</sup>, 69%<sup>2</sup>, and 83%<sup>3</sup> increased risks of heart disease
- Typically fail to account for saturated fat intake, intake of whole eggs vs. egg without yolks, and methods of preparation which confounds interpretation
- ***Well-controlled, clinical studies with heart disease endpoints or using surrogate markers (e.g., serum lipids) are needed***

# Early recommendations to general public: oversimplification of relationship

↑ cholesterol in food



↑ cholesterol in blood



Several  
decades

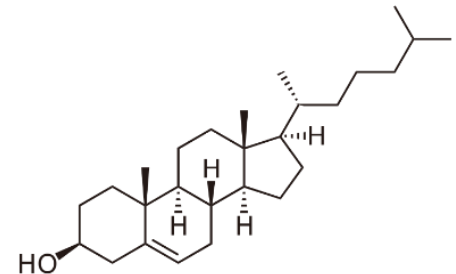
↑ heart disease



**Much more complicated than this...**

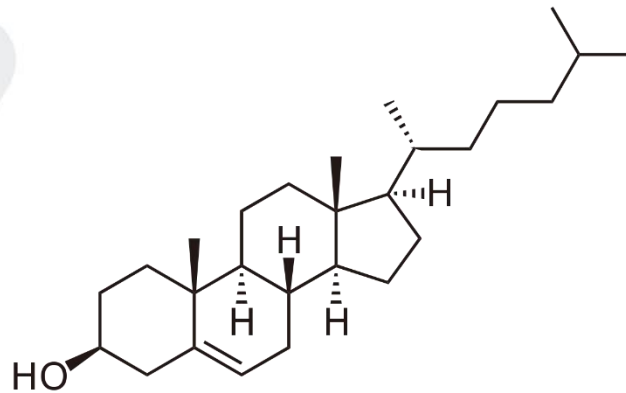
# Whole body cholesterol metabolism

- Only about 25% of serum cholesterol derived from diet
- ***The rest is derived from endogenous synthesis***
- Total body cholesterol synthesis: 840 mg/day
- Dietary cholesterol: 400 mg/day
- Absorb about 60%: 240 mg/day
- Total: 1080 mg/day
- 78% synthesis and 22% from diet





# What is the impact of dietary cholesterol on serum cholesterol in humans?



# Serum cholesterol response to dietary cholesterol

**Table 1.** Predicted plasma cholesterol response to a 100 mg/day change in dietary cholesterol

Reference:	$\Delta$ Plasma Cholesterol (mg/dL)	
Hegsted <i>et al.</i> 1965 [23]	4.5	
Keys <i>et al.</i> 1965 [24]	2.5	
Keys 1984 [25]	2.5	
Hegsted 1986 [26]	4.0	About 2.2-2.5 mg/dL change in serum cholesterol per 100 mg dietary cholesterol
NIH 1988 [27]	4.0	
McNamara 1990 [20]	2.2	
Hegsted <i>et al.</i> 1993 [28]	2.7	
Hopkins 1992 [29]	2.5	<b><i>One egg per day: ↑2-3%</i></b>
McNamara 1995 [30]	2.5	
Clarke <i>et al.</i> 1997 [21]	2.5	
Howell <i>et al.</i> 1997 [22]	2.2	
McNamara 2000	2.2	

“For the ***purpose of controlling the serum level***, dietary cholesterol should not be completely ignored but ***attention to this factor alone accomplishes little***” – Dr. Ancel Keys, 1965

# Adaptations to dietary cholesterol intake

- Why such a small change?
- Relatively precise feedback control mechanisms
  - ↑ dietary cholesterol: ↓ cholesterol absorption, ↓ cholesterol synthesis, ↑ cholesterol excretion
- “Egg man” – 88-yr old consumed 20-30 eggs/day with normal serum cholesterol (200 mg/dL)
  - Absorbed only 18% of dietary cholesterol



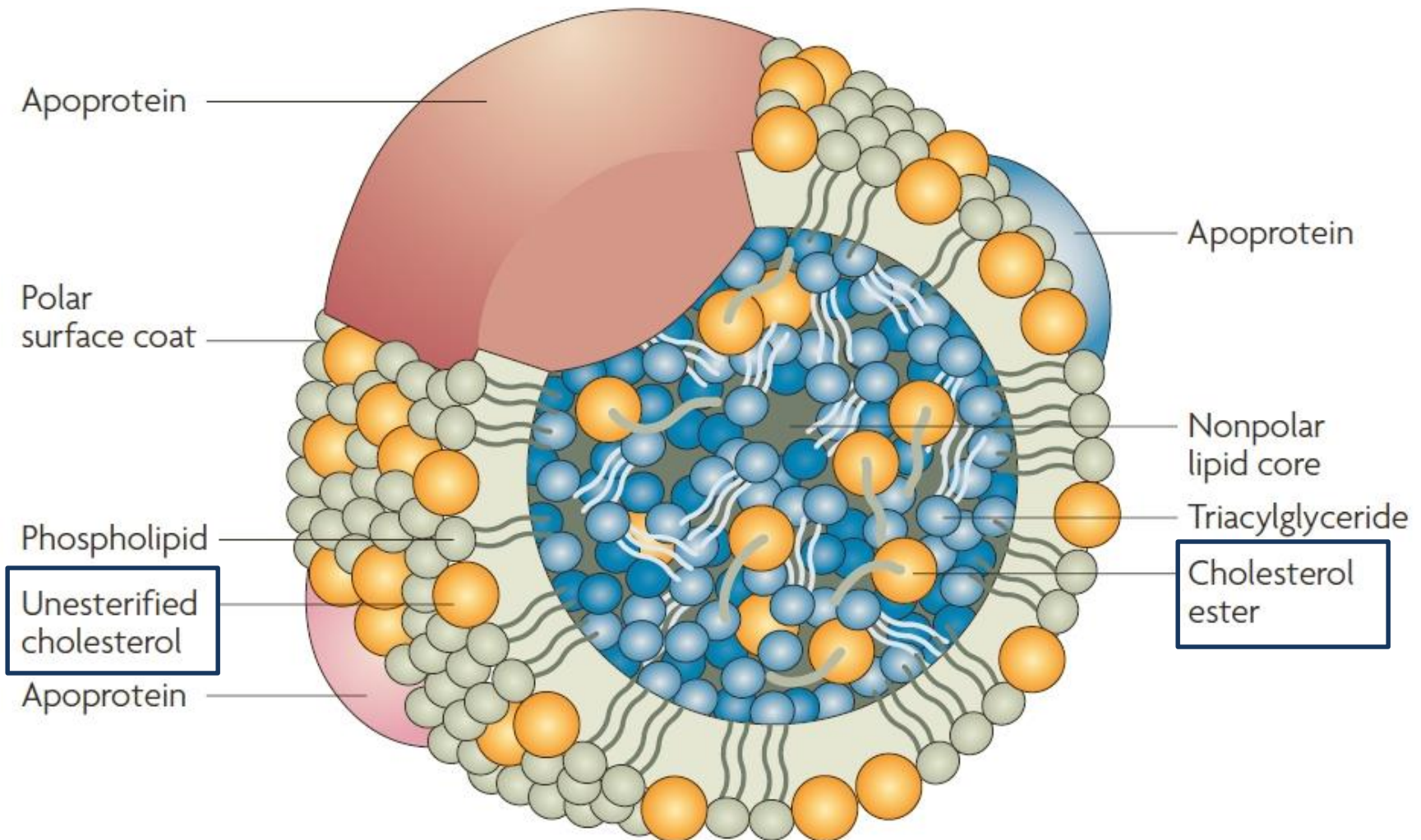
# Significant variability in serum cholesterol response to dietary cholesterol

- Not everyone reacts the same to dietary cholesterol
  - Response is highly variable and depends on genetic and metabolic factors

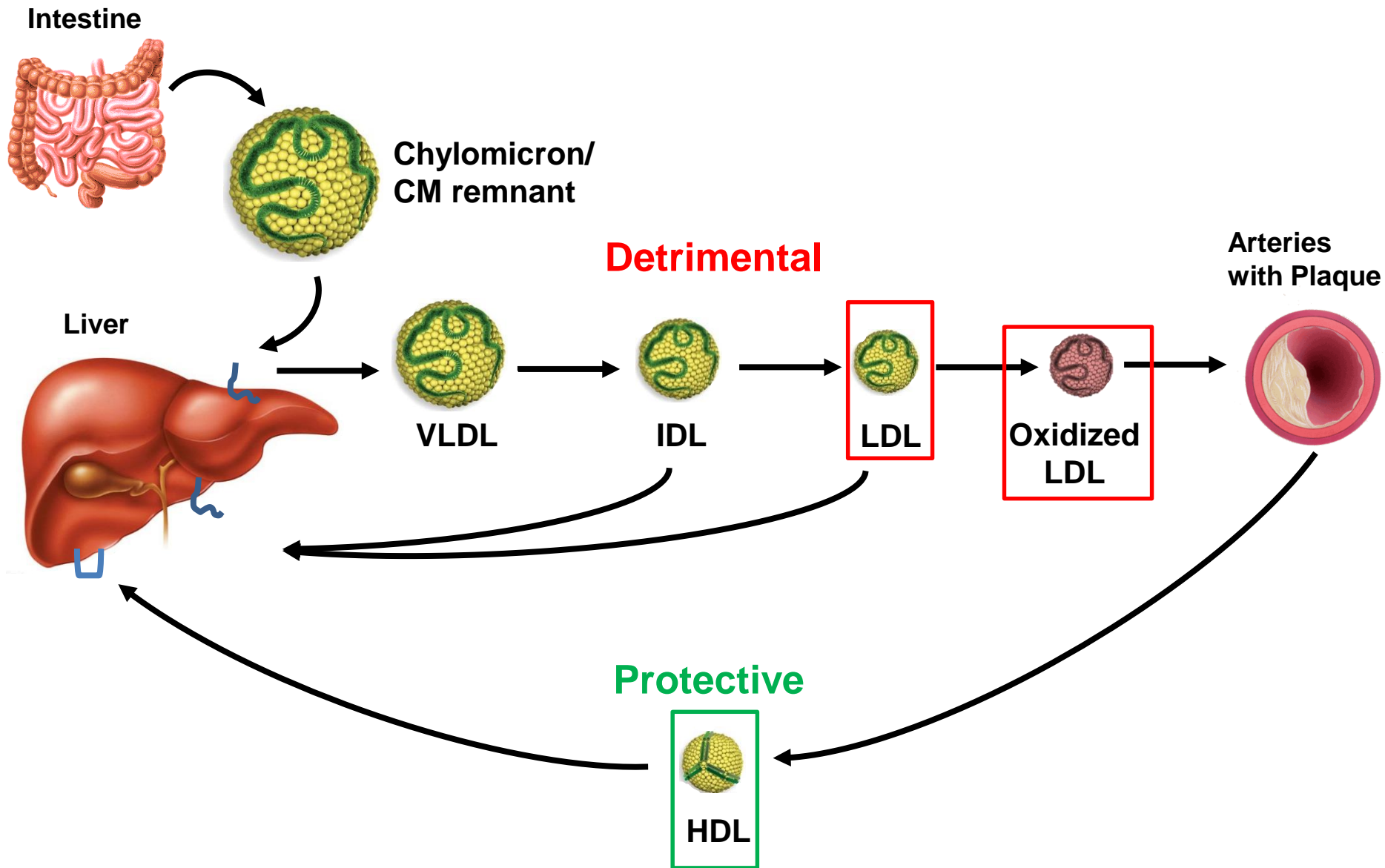


- Hyporesponders (compensators): 75-85% of population – no alteration or mild increase
- Hyperresponders (non-compensators):  $\geq 2.3$  mg/dL - 15-25% of population

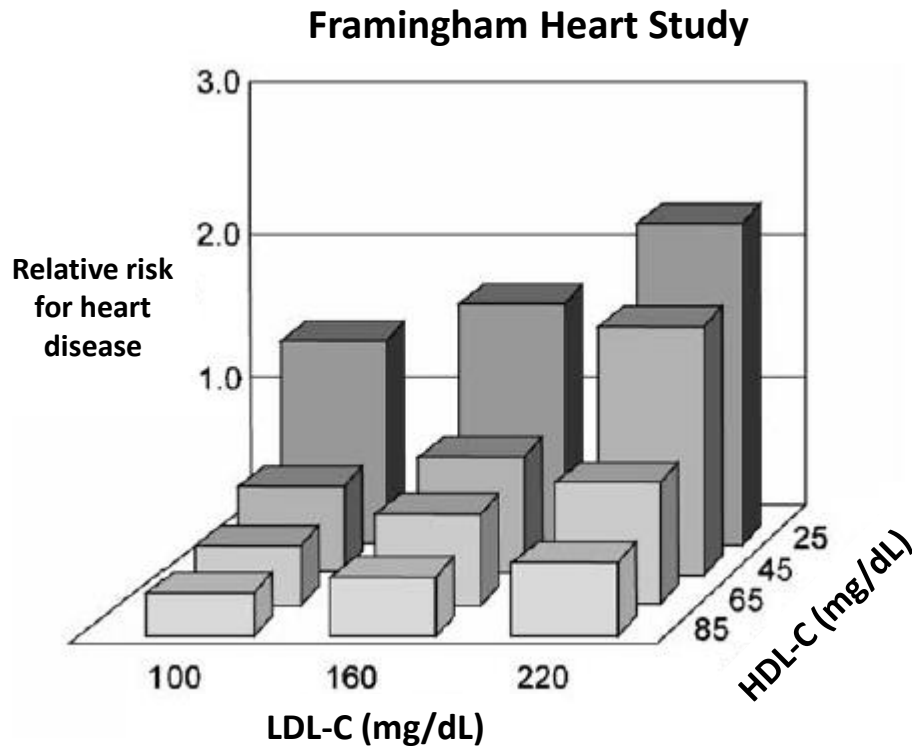
# Lipoproteins: transport vehicles for cholesterol in blood



# Role of cholesterol-carrying lipoproteins in heart disease



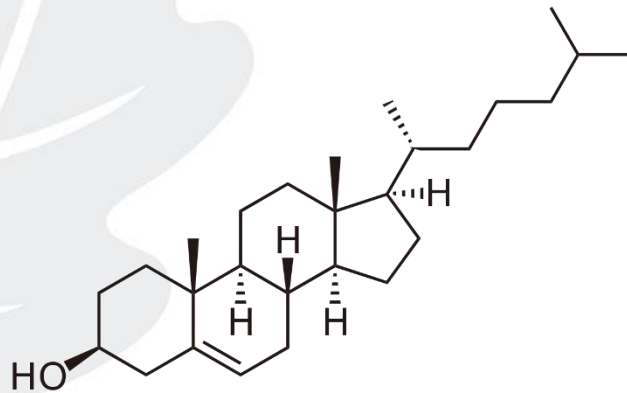
# Cholesterol levels as therapeutic targets for heart disease



- LDL-cholesterol (LDL-C): primary target of therapy for heart disease
- HDL-cholesterol (HDL-C): protective against heart disease

***LDL-C/HDL-C ratio important***

# How does egg intake affect LDL, HDL, and the LDL/HDL ratio?





# Egg intake during weight maintenance: healthy and hyperlipidemic populations



Study	Design	# days	LDL-C	HDL-C	LDL/HDL
<b>Children</b>					
Ballesteros et al. 2004	2 eggs per day vs. egg substitute	30	↑	↑	↔
<b>Adults</b>					
Herron et al. 2002 Healthy women	3 eggs per day vs. egg substitute	30	Hyperresponders: ↑ Hyporesponders: ↔	Hyperresponders: ↑ Hyporesponders: ↔	↔
Greene et al. 2005 Healthy elderly men/women	3 eggs per day vs. egg substitute	30	↑	↑	↔
Knopp et al. 2003 Insulin-sensitive	4 eggs per day vs. egg substitute	28	↑	↑	ND**
<b>Hyperlipidemic</b>					
Knopp et al. 1997 Hypercholesterolemic (HC) and combined hyperlipidemic (CHL) men/women	2 eggs per day vs. egg substitute	84	HC: ↔ CHL: ↑	↑	ND
Vishwanathan et al. 2009 Statin-taking elderly	2 or 4 eggs per day vs. egg exclusion	35	2 eggs: ↔ 4 eggs: ↑	↑	↔

\*\*not determined

# Egg intake during weight maintenance: insulin-resistant and diabetic populations



Study	Design	# days	LDL-C	HDL-C	LDL/HDL
<b><i>Insulin-resistant</i></b>					
Knopp et al. 2003 insulin-resistant (IR), obese insulin-resistant (OIR)	4 eggs per day vs. egg substitute	28	IR: ↔ OIR: ↔	IR: ↑ OIR: ↑	ND**
<b><i>Diabetic</i></b>					
Ballesteros et al. 2015 Diabetic patients	1 egg per day vs. oatmeal breakfast	35	↔	↔	↔
Fuller et al. 2015 Diabetic patients	2 eggs per day vs. egg exclusion	42	↔	↔	ND



\*\*not determined

# Egg intake during weight loss



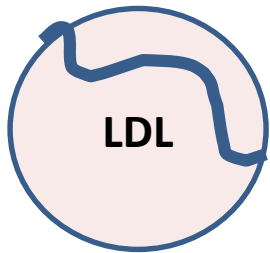
Study	Design	# days	LDL-C	HDL-C	LDL/HDL
Harman et al. 2008 Men/women	2 eggs per day vs. egg exclusion	84	↔	↔	ND**
Mutungi et al. 2008 Overweight/obese men	3 eggs per day vs. egg substitute	84	↔	↑	↔
Pearce et al. 2011 Diabetic patients	2 eggs per day vs. egg exclusion	84	↔	↑	↔
Blesso et al. 2013 Metabolic syndrome men/women	3 eggs per day vs. egg substitute	84	↔	↑	↓



\*\*not determined

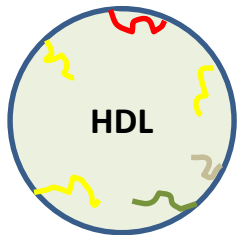
# LDL and HDL particle characteristics are related to heart disease

## “Healthy” LDL and HDL



↑ LDL size

- Weak link with heart disease

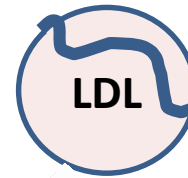


↑ Total HDL

↑ HDL size

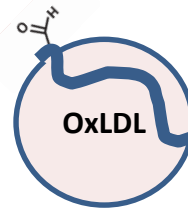
- Large HDL strongly protective

## “Heart disease” LDL and HDL



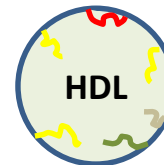
↑ Total and small, dense LDL

- Strong link with heart disease



↑ Oxidized LDL

- Highly atherogenic



↓ Total HDL

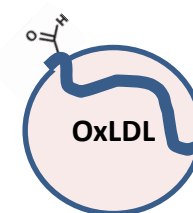
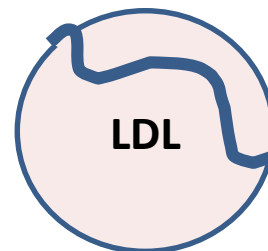
↓ HDL size

- “Dysfunctional”

# Effects of egg intake on lipoprotein atherogenicity



Study	Design	# days	LDL particles	Oxidized LDL	HDL particles
<b>Weight maintenance</b>					
Ballesteros et al. 2004 Children	2 eggs per day vs. egg substitute	30	↑ Large LDL ↑ LDL size ↓ Small LDL	ND**	ND
Herron et al. 2004 Healthy men/women	3 eggs per day vs. egg substitute	30	↑ Large LDL	↔	ND
Greene et al. 2006 Healthy elderly men/women	3 eggs per day vs. egg substitute	30	↑ Large LDL	ND	↑ Large HDL ↑ HDL size
Ballesteros et al. 2015 Diabetic patients	1 egg per day vs. oatmeal breakfast	35	↔	↔	↔
<b>Weight loss</b>					
Mutungi et al. 2008 Overweight/obese men	3 eggs per day vs. egg substitute	84	↑ Large LDL	ND	↑ Large HDL ↑ HDL size
Blesso et al. 2013 Metabolic syndrome men/women	3 eggs per day vs. egg substitute	84	↑ Large LDL	↔	↑ Large HDL ↑ HDL size



\*\*not determined

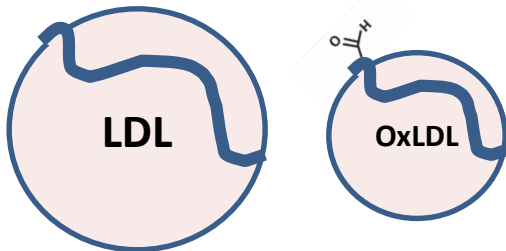
# Summary of egg effects on LDL and HDL metabolism

## LDL metabolism

↑ LDL-C in hyperresponders, ↔ LDL-C during weight loss

Shifts LDL particles: ↓ strongly atherogenic small LDL, ↑ less atherogenic large LDL

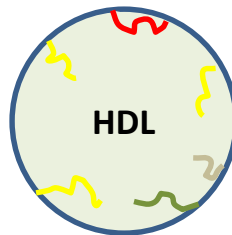
↔ oxidized LDL



## HDL metabolism

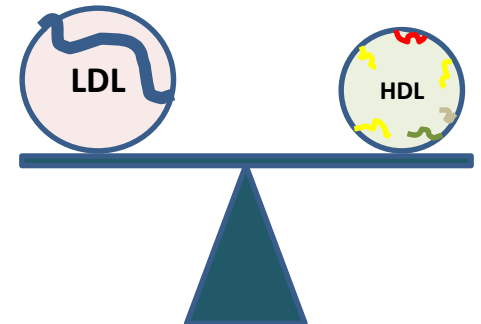
↑ HDL-C, especially with weight loss

↑ protective large HDL particles



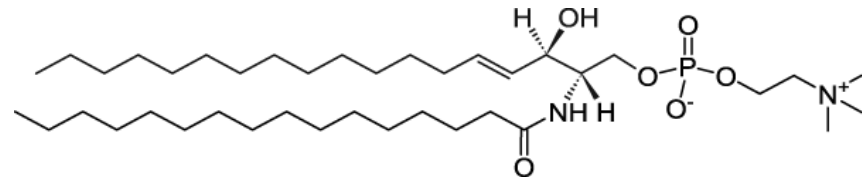
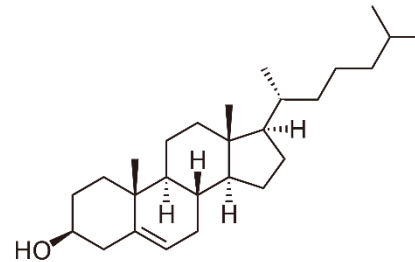
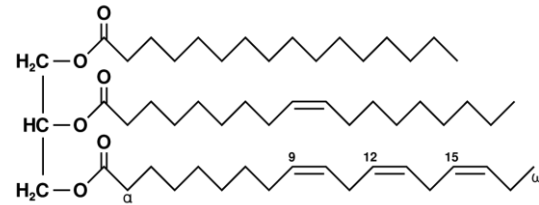
## LDL/HDL ratio

Maintains ratio during weight maintenance and weight loss



# Eggs are much more than cholesterol

- Types of lipids in eggs
  - Triglycerides
  - Sterols
    - Cholesterol
  - Phospholipids
    - Sphingomyelin



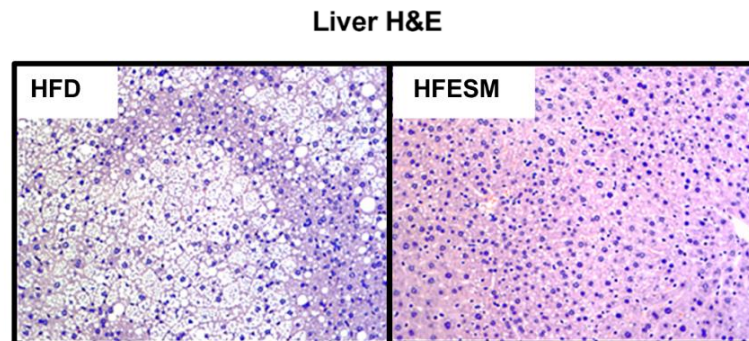
***All of the above serve different purposes in the foods we eat and can interact to affect our health***

# Dietary egg sphingomyelin is lipid-lowering in mice

10-wk high fat, high cholesterol diet (60% kcal fat; 0.2% cholesterol) (HFD)  
vs. HFD + 0.1% egg sphingomyelin by weight (HFESM)



- Adding egg sphingomyelin at a similar ratio to dietary cholesterol found in egg yolk
- ***Reductions in serum cholesterol (-22%) and liver triglyceride (-60%) and liver cholesterol (-24%)***





# Acknowledgments

## University of Connecticut

### Nutritional Sciences

Maria-Luz Fernandez, PhD

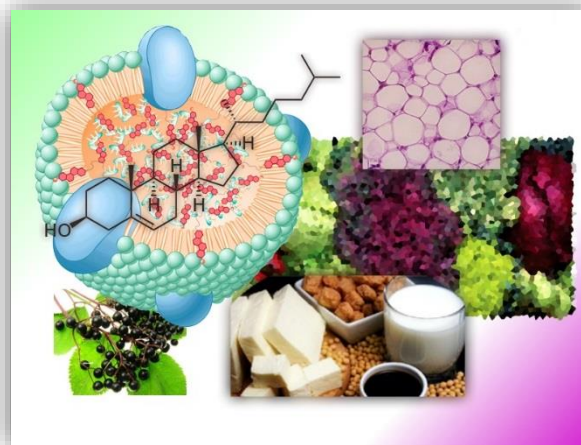
Ji-Young Lee, PhD

Gregory Norris

Caitlin Porter

Christina Jiang

Courtney Millar



## Blesso Laboratory



**UConn**  
COLLEGE OF AGRICULTURE,  
HEALTH AND NATURAL  
RESOURCES

NUTRITIONAL SCIENCES

## Fairfield University

### Biology

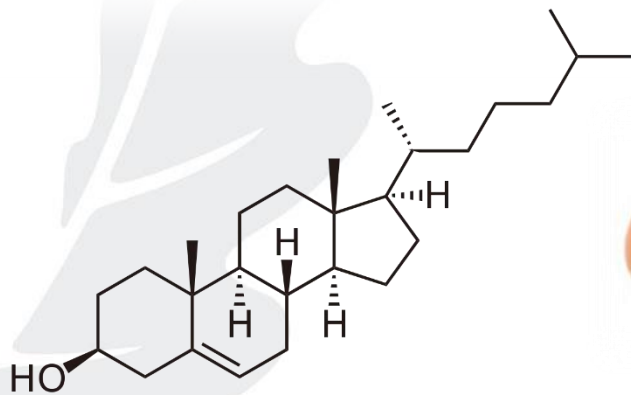
Catherine Andersen, PhD, RD



Egg Nutrition Center



***Thank you for your  
attention***



**UConn**