

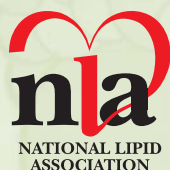
CLM-SAP™

■ **Edition 13**

Challenging Cases in Dyslipidemia

Complex Lipid Management Self-Assessment Program

Multiple True-False Questions Assessment
& Educational (Learning) Critiques



THIS CME/CE ACTIVITY IS SPONSORED BY:

THE NATIONAL LIPID ASSOCIATION

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Complex Lipid Management Self-Assessment Program (CLM-SAP™)

■ Edition 13, Complex Cases in Dyslipidemia

Target Audience:

Clinical Lipidologists, Cardiologists, Endocrinologists, Nephrologists, Primary Care Physicians, General Internists, Family Practitioners, Ph.D.s, Cardiovascular Nurses, Pharmacists, Physician Assistants, and Registered Dietitians.

Release Date: November 30, 2009

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Expiration Date: November 30, 2012

The estimated time for completion of this activity is 2.5 hours. There is no fee to participate and receive credit. This CME activity was planned and produced in accordance with ACCME Standards.

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Dear Healthcare Professional:

You are invited to participate in the Complex Lipid Management Self-Assessment Program (CLM-SAP™) Series Edition 13, *Challenging Cases in Dyslipidemia*. Edition 13 of CLM-SAP is part of a series designed to help you strengthen and reinforce your knowledge of clinical lipidology.

Edition 13 of CLM-SAP is sponsored by the National Lipid Association (NLA) for up to 2.5 *AMA PRA Category 1 Credits™* and by AKH Inc., Advancing Knowledge in Healthcare for Continuing Education Credit. The credits earned can be applied toward meeting the requirements necessary to be eligible for the American Board of Clinical Lipidology (ABCL) and the Accreditation Council for Clinical Lipidology (ACCL) Certifying Examinations.

This CLM-SAP was designed with medical specialty board technology to assess and strengthen your knowledge and provide you with an in-depth learning experience towards better understanding the options available for managing patients with complex dyslipidemia. The multiple true-false question component of the CLM-SAP was developed at the upper level of difficulty similar in type and format to a board certifying examination. Once you have properly completed Edition 13 in its entirety (see General Instructions below), your knowledge and competency in the management of patients with complex dyslipidemia will be strengthened.

General Instructions for Completion of CLM-SAP

Edition 13 of CLM-SAP consists of the following components:

■ Multiple True-False Questions (MCQs) Assessment Component

This consists of 20 multiple true-false MCQs (Items) which require that you respond either T (true) or F (false) to each of the three, four, or five lettered options for each item. Appendices I through III on pages 14–16 are relevant to completion of the MCQs.

■ Computer-Scored Answer Sheet

This is located on page 27. Please detach it along the perforation. Your selection of either TRUE or FALSE for *each* lettered option in each Item is to be marked on the answer sheet adjacent to the number for that Item. Please refer to the sample for how to mark your answers on the answer sheet.

■ Educational (Learning) Critiques Component

TO MAXIMIZE YOUR LEARNING EXPERIENCE IT IS IMPORTANT THAT YOU DO NOT LOOK AT THE EDUCATIONAL CRITIQUES COMPONENT UNTIL AFTER YOU HAVE COMPLETED MARKING YOUR ANSWERS FOR THE MCQs ON THE ANSWER SHEET. The critiques component contains detailed explanations for the correct and incorrect answers for the MCQs based on the most current peer-reviewed published information. Once you have read the Educational Critiques, the bibliographic references should be utilized as follow-up study for those MCQs that you answered incorrectly. The critiques are the teaching and learning component of CLM-SAP. They are to be used in combination with the MCQ assessment component to provide you with a *positive, active learning experience*.

DO NOT CHANGE THE ANSWERS MARKED ON YOUR ANSWER SHEET WHILE READING THE CRITIQUES. THE INTENT OF CLM-SAP IS LEARNING NEW KNOWLEDGE AND REINFORCING PREVIOUSLY LEARNED KNOWLEDGE. THERE IS NO PASS-FAIL SCORE.

■ Program Evaluation Component

After you have completed the MCQ and Critique components as instructed on page 2, turn to the reverse side of your computer-scored answer sheet. Please select the one lettered option that BEST answers each program evaluation question and mark it on the answer sheet. Then indicate the number of hours for which you are claiming CME or CE credit, and sign the form.

Note

After you have completed sections A and B of the answer sheet, it is important that you return it to the National Lipid Association (NLA) by Fax to: 904.998.0855 or Mail to: NLA, 6816 Southpoint Parkway, #1000, Jacksonville, FL 32216. To receive a statement of credit from the NLA for up to 2.5 *AMA PRA Category 1 Credits™* or from AKH Inc. for continuing education credit, you must return your completed answer sheet and signed program evaluation form. PLEASE ALLOW 6–8 WEEKS FOR RECEIPT OF YOUR STATEMENT OF PARTICIPATION. In addition, by returning your completed answer sheet, your participation will be documented for future certification purposes.

Educational Objectives

After completing this enduring materials CME/CE activity, you will be better able to:

- Manage complex cases of dyslipidemia including a patient with severe hypertriglyceridemia; a patient with tendon xanthomas but no family history of heart disease; a low risk patient with elevated hs-CRP; a patient with statin intolerance; a patient with normal lipid profile but with a strong family history of premature CHD; and a patient with recent acute coronary syndrome and metabolic syndrome.
- Discuss the etiology of various types of complex dyslipidemia and the role of biomarkers.
- Recognize gene variations associated with complex dyslipidemia.

Accreditation



Physicians: The National Lipid Association (NLA) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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In accordance with the ACCME Standards for Commercial Support, ACPE, ANCC, and CDR policies and standards and the policy of the NLA, any faculty relationship with the manufacturer(s) of any commercial product(s) discussed in this educational activity, which in the context of their presentation could be perceived as a real or apparent conflict of interest (e.g., ownership of stock, honoraria, research grants, or consulting fees), is disclosed below.

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Michael H. Davidson, M.D., FACC, FACP

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None.

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Complex Lipid Management Self-Assessment Program (CLM-SAP™)

Multiple True-False Questions (MCQs)

Directions

Items 1–20 require that you answer either TRUE or FALSE for each option (A through E) in EACH item by filling in the corresponding circle on the answer sheet found in the back of the book. The sample to the right illustrates how to do this.

1	
T	F
(A) ●	●
●	(B)
●	(C)
●	(D)
(E)	●

■ Items 1–5

A Young Woman with Severe Hypertriglyceridemia

A 35-year-old woman presents to the lipid clinic upon referral by her OB/GYN physician for evaluation of severe hypercholesterolemia. Her past medical history is unremarkable. Both her parents died with premature CHD (father age 58 and mother age 57). She is 5'6", 198 lbs. She had difficulty with fertility and, with therapy, delivered healthy triplets. During pregnancy, she had gestational diabetes. After her pregnancy, she continued to gain a considerable amount of weight and now weighs 60 lbs. more than her pre-pregnancy weight. A lipid profile performed four weeks prior to her visit was total cholesterol >1000 mg/dL (verified by repeat analysis, highest level of detection) and triglycerides (TG) 4544 mg/dL (also verified by repeat measures). HDL and LDL-C were not performed due to the fact that specimen was unsuitable for assay due to lipemia. She was placed on fenofibric acid 135 mg and prescription omega-3 fatty acids 4 g/day and referred to you for further evaluation. Her repeat lipid profile was as follows:

Total Cholesterol	643 mg/dL
Triglycerides	1277 mg/dL
HDL-C	N/A
LDL-C	N/A
Glucose	108 mg/dL
AST	23 u/L (N = 10–30 u/L)
ALT	30 u/L (N = 6–40 u/L)

1. Which of the following physical findings depicted in photographs A–E is/are consistent with this patient’s medical history and laboratory findings?



(A)



(B)



(C)



(D)



(E)

2. Which of the following tests is/are appropriate for this patient?

- (A) Apo E genotype.
- (B) A1C.
- (C) Pelvic ultrasound.
- (D) TSH.
- (E) C-peptide.

Results of the tests were as follows: Apo E genotype — 2:2; A1C — 6.1%; pelvic ultrasound — ovarian cyst; TSH — 2.0 μ /L; and c-peptide — normal.

3. Based on all of the information that you now have, which of the following is/are appropriate treatments for this patient?

- (A) Low glycemic index/low carbohydrate diet.
- (B) Atorvastatin 40 mg.
- (C) Metformin.
- (D) Colesevelam.
- (E) Niacin.

4. She is placed on dietary therapy and 2 medications. She wants to get pregnant. Which of the following medications would need to be discontinued?

- (A) Fenofibrate.
- (B) Atorvastatin.
- (C) Metformin.
- (D) Prescription omega-3.
- (E) Gemfibrozil.

5. Her husband has a normal lipid profile and his Apo E genotype is 3:3. Which of the following statements is/are true?
- (A) The chance their child will have familial dysbetalipoproteinemia is 50%.
 - (B) The American Academy of Pediatrics recommends nutritional therapy with reduced-fat milk at 1 year for children at risk owing to obesity or family history.
 - (C) Pregnancy is not associated with an increased risk of pancreatitis in patients with familial dysbetalipoproteinemia.
 - (D) The American Diabetes Association recommends that all pregnant women have a 75 g glucose load oral glucose tolerance test to rule out gestational diabetes.
 - (E) Women with gestational diabetes should be screened for diabetes 6-12 weeks post partum and should be followed up with subsequent screening for the development of diabetes or pre-diabetes.

■ Items 6–7

A Patient with Tendon Xanthomas but No Family History of Heart Disease

A 22-year-old woman is referred to you after having a large tendon xanthoma removed from her wrist. She had a cataract removed from her left eye two years ago. Both her parents are alive and well with no history of coronary heart disease.



6. Which of the following mutations is/are associated with the presence of tendon xanthoma?
- (A) LDL receptor binding domain abnormality.
 - (B) Apo B R3500Q.
 - (C) PCSK9 upregulation.
 - (D) 7-alpha-hydroxylase deficiency.
 - (E) ABCG8 deficiency.
7. Both of her parents have a normal lipid profile. Which of the following genetic diseases is/are possible in this patient?
- (A) Autosomal recessive hypercholesterolemia.
 - (B) Familial hypercholesterolemia.
 - (C) Beta sitosterolemia.
 - (D) Cerebrotendinous xanthomatosis (CTX).
 - (E) Familial defective Apo B.

■ Items 8–10

A Relative Low Risk Woman with Elevated hs-CRP

A 60-year-old college professor comes to see you for an opinion as to whether she should initiate statin therapy. Her lipid profile is as follows:

Total Cholesterol	201 mg/dL
Triglycerides	150 mg/dL
HDL	45 mg/dL
LDL	126 mg/dL
Glucose	99 mg/dL

Vitals:	
Blood Pressure	120/78 mm Hg
Height	5'2"
Weight	130 lbs
Waist circumference	36"

Her father died at age 66 of pancreatic cancer and her mother, age 83, had coronary bypass surgery ten years ago and she has type 2 diabetes mellitus. A brother, age 62, had a stent placed in his left anterior descending artery at age 58. She recently had an hs-CRP of 4.5 mg/L; she takes no medications.

8. Regarding the JUPITER trial, which of the following statements is/are true for this patient?
- (A) She would have qualified for participation.
 - (B) Women did not achieve a significant reduction in the primary endpoint.
 - (C) There was a significant increase in the development of type 2 diabetes in patients treated with rosuvastatin.
 - (D) The incidence of venous thrombosis was decreased in patients on rosuvastatin.
 - (E) Rosuvastatin was associated with an increase in cancer mortality.

After discussing the results of the JUPITER trial with her, she decides to start rosuvastatin 20 mg qd. The results of her laboratory tests were as follows:

Total Cholesterol	140 mg/dL
Triglycerides	130 mg/dL
HDL-C	48 mg/dL
LDL-C	66 mg/dL
hs-CRP	3.2 mg/L

9. Which of the following drugs has/have been demonstrated in clinical trials to lower hs-CRP when added to statin therapy?
- (A) Ezetimibe.
 - (B) Fenofibric Acid.
 - (C) Niacin.
 - (D) Omega-3 fatty acid.
 - (E) Colesevelam.

10. Which of the following statements is/are true regarding dual targets for lipids and hs-CRP in the JUPITER trial?
- (A) Compared with placebo, participants allocated to rosuvastatin who did not achieve LDL-C <70 mg/dL had no significant reduction in vascular events.
 - (B) Participants who achieved an LDL-C <70 mg/dL had similar vascular event rates if the hs-CRP was either <2 mg/L or <1 mg/L.
 - (C) For participants who achieved an Apo B to Apo A-1 ratio <0.5, an hs-CRP <2 mg/L did not predict better clinical outcomes.
 - (D) Participants who achieved >50% hs-CRP reduction had fewer vascular events than those who had <50% hs-CRP reduction.
 - (E) Participants allocated to rosuvastatin who did not achieve an hs-CRP <2 mg/L did not have a significant reduction in vascular events.

■ Items 11–13

Statin Intolerance

A 68-year-old woman with type 2 diabetes mellitus presents to the lipid clinic with statin intolerance. She has tried atorvastatin, rosuvastatin, simvastatin, and fluvastatin but after each therapy, stopped due to profound muscle weakness. Her CK levels have always been normal. Her present medications include ezetimibe 10 mg qd, metformin 1500 mg/day, pioglitazone 30 mg qd, and synthetic thyroid replacement 0.25 mg qd. Results of her laboratory tests are as follows:

Total Cholesterol	250 mg/dL
Triglycerides	100 mg/dL
HDL-C	40 mg/dL
LDL-C	190 mg/dL
Glucose	128 mg/dL
A1C	6.9%

11. Which of the following is/are risk factors for statin intolerance?
- (A) Hypothyroidism.
 - (B) Family history of statin intolerance.
 - (C) SLCO1B1 variant.
 - (D) Elderly – age >65.
 - (E) Vitamin D deficiency.
12. Which of the following drugs has/have been demonstrated to lower LDL-C by at least an additional 5% in combination with ezetimibe?
- (A) Colesevelam.
 - (B) Fenofibrate.
 - (C) Omega-3 fatty acid.
 - (D) Pioglitazone.
 - (E) Niacin.

Her TSH is 6.0 u/mL and her vitamin D level is 10 u/L.

13. Which of the following statements is/are true regarding this patient?
- (A) Increasing the dose of the synthetic thyroid replacement will further decrease the LDL-C.
 - (B) Vitamin D replacement has been shown to improve statin intolerance.
 - (C) Red yeast rice lowers the LDL-C by approximately 20%.
 - (D) Twice a week rosuvastatin has been shown to be tolerated in patients with statin intolerance.
 - (E) This patient would be considered eligible for LDL apheresis according to Medicare guidelines.

■ Items 14–15

Strong Family History of Premature CHD with Normal Lipid Profile

A 30-year-old man presents to the lipid clinic for evaluation of cardiovascular risk. Both his father and grandfather died of myocardial infarctions in their 40's. His mother, age 52, is alive and "healthy". He is 5'10", weighs 210 lbs., waist circumference 37", blood pressure 148/98 mm Hg. He is well with no clinical heart disease. His mother apparently has "high cholesterol" and takes atorvastatin 10 mg qd. He is the oldest of four children and his siblings reportedly have no "cholesterol problems". His last lipid profile was five years ago and he was told it was "normal". He wants a complete evaluation to find out if he is at increased risk for heart disease. He got married one year ago and his wife recently gave birth to a healthy son.

14. Which of the following genes or polymorphisms is/are associated with increased risk of CHD?
- (A) 9P21.
 - (B) KIF6 gene variant.
 - (C) PCSK9 deficiency.
 - (D) Lp(a).
 - (E) Apo A-II overproduction.
15. Which of the following biomarkers is/are associated with an increased risk for development of type 2 diabetes over a 5-year period?
- (A) hs-CRP.
 - (B) Insulin.
 - (C) Ferritin.
 - (D) Adiponectin.
 - (E) Small dense LDL.

■ Items 16–20

A Patient with Recent Acute Coronary Syndrome and Metabolic Syndrome

A 55-year-old Hispanic woman is referred to your lipid clinic for evaluation and treatment of her dyslipidemia. She recently had a stent placed in the right coronary artery after she developed unstable angina. She is 5'2", weight 130 lbs., waist circumference 36". Medications include simvastatin 40 mg, clopidogril 75 mg, aspirin 81 mg, ramipril 5 mg. Her blood pressure is 120/70 mm Hg. Her lipid profile is as follows:

Total Cholesterol	160 mg/dL
Triglycerides	300 mg/dL
HDL-C	32 mg/dL
LDL-C	68 mg/dL
LDL-P	1200 nmol/L
HDL-P	25 nmol/L
LDL size	18 nm
HDL size	8.0 nm
Apo B	89 mg/dL
hs-CRP	2.9 mg/L

16. Which of the following statements is/are true regarding this patient?
- (A) According to an analysis of the TIMI-22 (PROVE-IT) trial, there was an increased risk in patients with acute coronary syndrome and the on-treatment LDL was <70 mg/dL if either the hs-CRP was >2.0 mg/L or TGs were >150 mg/dL.
 - (B) According to the NCEP ATP IV 2004 Update, she is at goal for lipid levels.
 - (C) According to the ADA/ACC Consensus Statement on the management of patients with cardiometabolic risk, she is at her target for Apo B of <90 mg/dL.
 - (D) In the Framingham Study, if the LDL-P were high but the LDL-C were low, the event-time survival was similar to those if the LDL-P were low but the LDL-C were high.
 - (E) Lp-PLA2, an enzyme involved in atherogenesis, seems to be preferentially associated with circulating LDL particles that are small, dense, TG-enriched, and carrying an electronegative charge.
17. In regards to the addition of prescription omega-3 fatty acids 4 g/day to this patient's treatment, which of the following changes is/are to be expected?
- (A) Increase in Apo A1.
 - (B) Decrease in Lp-PLA2.
 - (C) Increase in Apo C-III.
 - (D) Decrease in RLP-C.
 - (E) Decrease in large VLDL.

- 18.** Regarding the addition of fenofibric acid 135 mg to this patient's treatment, which of the following changes is/are to be expected:
- (A) Increase in Apo A-1.
 - (B) Decrease in Apo B.
 - (C) Decrease in Apo C.
 - (D) Decrease in hs-CRP.
 - (E) Decrease in homocysteine.
- 19.** Regarding the addition of niacin 2 gm/day to this patient's treatment, which of the following laboratory results is/are to be expected?
- (A) Increase in HDL-C by 30%.
 - (B) Decrease in Lp(a).
 - (C) Decrease in homocysteine.
 - (D) Decrease in RLP.
 - (E) Increase in HDL3 (small) more than HDL2 (large).
- 20.** In regards to lipoprotein particle concentration and size, which of the following statements is/are true?
- (A) In the EPIC-Norfolk cohort, both HDL size and HDL particle concentration were independently associated with the risk of CHD.
 - (B) Omega-3 fatty acids increase LDL particle size but does not decrease LDL-P particle number.
 - (C) In the IDEAL trial, the Apo B/A-1 ratio was the most predictive of all lipid parameters for CHD events.
 - (D) Non-HDL-C correlates better with Apo B than does LDL-C.
 - (E) After adjusting for LDL-P, LDL size does not predict future CHD events.

Complex Lipid Management Self-Assessment Program (CLM-SAP™)

Appendices

■ Appendix I

Normal Laboratory Values (N) of Clinical Importance

Alanine transaminase (ALT), serum 3–50 U/L

Apo A-1, normal value: 80 mg/dL

Apo B, normal value: <90 mg/dL

Aspartate transaminase (AST), serum 5–55 U/L

Creatine phosphokinase (CK), serum 25–90 U/L (males),
10–70 (females)

Creatinine, serum, 0.6–1.3 mg/dL (males),
0.5–1.1 mg/dL (females)

C-reactive protein (CRP), plasma 0–6.2 mg/L

Gamma-Glutamyl Transferase (GGT), 50 μ /L

Glucose (fasting), plasma 90 mg/dL,
>100 mg/dL (diabetes mellitus)

Hemoglobin, glycosylated (A1C) <6% of total Hb

High density lipoprotein (HDL), <40 mg/dL

Homocysteine, plasma 14.2 μ mol/L

Large HDL-P, <4.0 μ mol/L (high risk)

Low density lipoprotein (LDL),
plasma <100 mg/dL (males and females)

LDL particle size, small pattern B \leq 20.5 nm

LDL-P (particle number), <1000 nmol/L (optimal)

LDL-S₃GGE®, LDL IIIa+IIIb% \leq 15%

LDL-S₃GGE®, LDL IVb% \leq 5%

LDL-S₁₀GGE®, HDL 2b% (M)>20%, (F)>30%

Lipoprotein (Lp(a)), plasma <30 mg/dL

Lp-PLA₂, 235 ng/ml

Lipase, lipoprotein (LPL), plasma 50–250 units/L

Thyroid Stimulating Hormone (TSH) 0.4–4 mIU/L

Total cholesterol (TC), plasma <200 mg/dL
(males and females)

Triglyceride (TG), serum <150 mg/dL

Very low density lipoprotein (VLDL), plasma <30 mg/dL

Vitamin D daily requirements, 100 IU/day (adults),
200 IU/day (infants and children), 400 IU/day
(pregnant/lactating)

■ Appendix II

List of Abbreviations Frequently Occurring in CLM-SAP™, Edition 13

A. Biochemical

ABC	ATP-binding cassette transporter
ACAT	acyl-CoA: cholesterol acyltransferase
ACE	angiotensin-converting enzyme
ACV	allograft coronary vasculopathy
A1C	hemoglobin, glycosylated
Apo	apolipoproteins/apoproteins
ALT	alanine transaminase
AST	aspartate transaminase
BAS	bile acid sequestrants
CETP	cholesteryl ester transfer protein
CK	creatine phosphokinase
CRP	C-reactive protein
CYP	cytochrome
EBCT	electron beam computed tomography
GGT	gamma glutamyl transferase
HDL	high density lipoprotein
HMG-CoA	3-hydroxy-3-methylglutaryl coenzyme A
HL	hepatic lipase
HRT	hormone replacement therapy
IBAT	ileal bile acid transporter
IDL	intermediate density lipoprotein
LCAT	lecithin: cholesterol acyltransferase
LDL	low density lipoprotein
Lp	lipoprotein
LPL	lipoprotein lipase
MTP	microsomal triglyceride transfer protein
PPAR	peroxisome proliferator-activated receptor
SAMs	statin-associated myalgias
SR	scavenger receptor
SSRI	selective serotonin re-uptake inhibitors
TSH	thyroid-stimulating hormone
TZD	thiazolidinediones
VLDL	very low density lipoprotein
ICAM	cell adhesion molecule inflammatory

B. Medical

AAA	abdominal aortic aneurysm
ABI	ankle-brachial index
ACV	allograft coronary vasculopathy
BMI	body mass index
CABG	coronary artery bypass graft
CHD	coronary heart disease
CVD	cardiovascular disease
CAD	coronary artery disease
COPD	chronic obstructive pulmonary disease
FH	familial hypercholesterolemia
IMT	intima-media thickness
LVH	left ventricular hypertrophy
MI	myocardial infarction
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel, Third Report
PAD	peripheral arterial disease
PCI	percutaneous coronary intervention
PCOS	polycystic ovarian syndrome
PTCA	percutaneous transluminal coronary angioplasty
PVD	peripheral vascular disease
TLC	therapeutic lifestyle changes

■ Appendix III

Cholesterol- and Lipid-Lowering Drug Classes and Generic/Trade Names

- A. Bile Acid Sequestrants (Resins)**
 - cholestyramine (LoCholest[®], Questran[®], Prevalite[®])
 - colestipol (Colestid[®])
 - colesevelam (Welchol[®])
- B. Fibric Acid Derivatives**
 - clofibrate (Atromid-S[®])
 - gemfibrozil (Lopid[®])
 - fenofibrate (Tricor[®])
- C. HMG-CoA Reductase Inhibitors (Statins)**
 - atorvastatin (Lipitor[®])
 - fluvastatin (Lescol-XL[®])
 - lovastatin (Mevacor[®])
 - pravastatin (Pravachol[®])
 - simvastatin (Zocor[®])
 - rosuvastatin (Crestor[®])
- D. Cholesterol Absorption Inhibitors**
 - ezetimibe (Zetia[®])
- E. Combination Therapy**
 - ezetimibe/simvastatin (Vytorin[®])
- F. Nicotinic Acid (Niacin)**
 - crystalline nicotinic acid (Niacor[®])
 - extended-release niacin (Niaspan[®])
- G. Prescription Omega-3 Fatty Acids**
 - concentrated ethyl ester omega-3 fatty acid (Lovaza[®])

Other Drug Classes and Generic/Trade Names

- clarithromycin (Biaxin[®])
- cyclosporine (Sandimmune[®], Neoral[®])
- amiodarone (Cordarone[®])
- enalapril (Vasotec[®])
- diltiazem (Cardizem[®], Dilacor XR[®])
- fluconazole (Diflucan[®])
- ketoconazole (Nizoral[®])
- rалoxifene (Evista[®])
- acarbose (Precose[®])
- glyburide (Micronase[®])
- glipizide (Glucotrol[®])
- metformin (Glucophage[®])
- pioglitazone (Actos[®])
- rifampin (Rifadin[®])
- rosiglitazone (Avandia[®])
- sirolimus (Rapamune[®])
- verapamil (Isoptin[®], Calan[®])
- indinavir (Crixivan[®])
- lamivudine (Epivir[®])
- ritonavir (Norvir[®])
- saquinavir (Invirase[®])
- nevirapine (Viramune[®])
- zidovudine (Retrovir[®])

Complex Lipid Management Self-Assessment Program (CLM-SAP™)

Educational (Learning) Critiques

Items 1–5 True Answers: 1 (A, B, C, E); 2 (A, B, C, D); 3 (A, B, C, E); 4 (A, B, C); 5 (A, B, E)

A Young Woman with Severe Hypertriglyceridemia

This 35-year-old woman has type III hyperlipidemia, familial dysbetalipoproteinemia (FDB), and the polycystic ovarian syndrome (PCOS). The diagnosis of type III hyperlipidemia is confirmed by the Apo E genotype of 2:2. The major metabolic defect in type III hyperlipidemia is an impaired remnant lipoprotein clearance secondary to a reduced affinity of Apo E-2 for the Apo B-E receptor (or LDL receptor). Apo E-2 has 1% of the affinity of Apo E-3 and Apo E-4 for the LDL receptor. The Apo E-2/2 phenotype in the presence of a second factor interfering with triglyceride-rich lipoprotein metabolism (i.e., a “second hit”, as in this case, PCOS) results in delayed chylomicron remnant and VLDL remnant (IDL) removal by the liver. Plasma levels of both cholesterol and triglycerides (TGs) can be extremely elevated due to the elevated IDL which has a cholesterol to triglyceride ratio of close to 1:1 (compared to the ratio of 1:5 in VLDL).

PCOS is linked to insulin resistance, diabetes, and obesity and due to the overproduction of VLDL, led to the severe hypercholesterolemia in this young woman with the underlying Apo E-2/2 phenotype. PCOS is an endocrine disorder that affects approximately 5% of all women and is a leading cause of infertility. Not all women with PCOS have polycystic ovaries nor do all women with ovarian cysts have PCOS. Pelvic ultrasound is a major diagnostic tool to look for small ovarian follicles, most likely associated with disturbed ovarian function with failed ovulation. To exclude other disorders, prolactin, TSH, and 7-alpha hydroxylase should be measured to rule out hyperprolactinemia, hypothyroidism, and 21-hydroxylase deficiency (CAH).

A c-peptide level, a marker of insulin production, would not be helpful diagnostically or affect treatment and, therefore, is not appropriate. The results of the laboratory tests taken in this woman are as follows: Apo E genotype — 2:2; A1C — 6.1%; pelvic ultrasound — ovarian cyst; TSH — 2.0 μ /L; and c-peptide — normal.



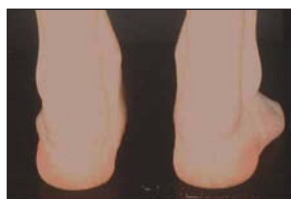
(A)



(B)



(C)



(D)



(E)

In regards to physical findings shown in the photos (A through E), this patient would most likely have tubero-eruptive xanthoma on the elbows and yellow deposits on the palm of her hands (photos A&B). She would be very unlikely to have tendon xanthomas, which is pathognomonic of familial hypercholesterolemia (photo D) because the TGs are markedly elevated. Type III hyperlipidemia requires a “second hit” to increase VLDL reduction, for example polycystic ovarian syndrome (PCOS) with the commonly associated hirsutism (photo C) or hypothyroidism, which results in loss of one-third of the eyebrow and puffy eyelid (photo E).

In regards to treatment for type III hyperlipidemia, statins are very effective. Atorvastatin 40 mg as monotherapy in 36 patients with type III decreased total cholesterol and TGs by 40% and 43%, respectively. A low glycemic/low carbohydrate diet is especially effective in patients with type III hyperlipidemia. (In this patient, after she was put on a low-carbohydrate diet, her total cholesterol decreased to 232 mg/dL, TGs to 400 mg/dL, LDL to 96 mg/dL, and HDL to 56 mg/dL.) Niacin is also an effective treatment for type III hyperlipidemia. Metformin would be a consideration because she has pre-diabetes and PCOS. Metformin has been shown to reduce the development of type 2 diabetes in patients with pre-diabetes and is a potential treatment to improve PCOS-related insulin resistance. Colesevelam, a bile acid sequestrant which increases VLDL production, would not be an appropriate treatment for type III hyperlipidemia.

In regards to drugs during pregnancy, fenofibrates, atorvastatin, and metformin are contraindicated. Prescription omega-3 fatty acids can be used during pregnancy; and DHA supplements taken during pregnancy are a safe and effective form of omega-3 fatty acid that avoids mercury intake (associated with birth defects) that may occur with excessive fish consumption. Gemfibrozil has been used during pregnancy in women with severe hypertriglyceridemia.

Since her husband has the Apo E phenotype E 3:3, there is no chance her triplets will be E 2:2 and, therefore, the chance of developing type III hyperlipidemia is 0% in her children. However, because of her history of obesity, it is appropriate that her children be placed on low-fat milk after one year based on a new recommendation by the American Academy of Pediatrics. Pregnancy is associated with an increased risk of pancreatitis in patients with type III hyperlipidemia. The ADA does not recommend an oral glucose tolerance test for all pregnant women but does recommend that women with gestational diabetes be followed up 6–12 weeks post partum to be screened for the development of pre-diabetes or diabetes.

Items 6–7

True Answers: 6 (A, B, C, D, E); 7 (A, C, D)

A Patient with Tendon Xanthomas but No Family History of Heart Disease

Although LDL receptor mutations leading to familial hypercholesterolemia are the most common cause of tendon xanthoma, there are other mutations that are associated with severe elevation of LDL; and there are other genetic causes of tendon xanthomas that are not caused by high LDL-C levels. The differential diagnosis of tendon xanthomas include the following:

1. Familial hypercholesterolemia (FH1) due to mutation of LDL receptor.
2. Familial defective Apo B-100 (FH2 or FDB) due to mutations of Apo B-100. The first to be recognized is Apo B-3500 (R3500Q).
3. Autosomal dominant familial hypercholesterolemia (FH3) due to an over expression of PCSK9. PCSK9 is a protein that promotes LDL receptor degradation. When PCSK9 is genetically overexpressed, there is enhanced degradation of LDL receptor leading to hypercholesterolemia. PCSK9 deficiency leads to low levels of LDL-C and lifelong protection from CHD.

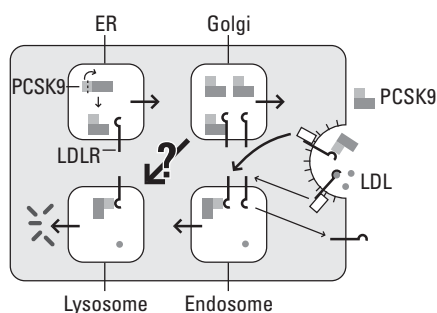


Figure 1. PCSK9 and LDLR Degradation

4. Autosomal recessive hypercholesterolemia (ARH). This recessive disorder (both parents are normolipidemic) is due to a mutation of protein that is necessary for the internalization of LDL after normal binding to the LDL receptor. In patients with ARH, LDL uptake in the liver is reduced as in patients with homozygous FH, thus promoting the development of clinical presentation of ARH. ARH is responsive to therapy such as, statins, bile acid sequestrants, and ezetimibe which work by upregulating the LDL receptor.
5. Dysbetalipoproteinemia (type III) is associated with tubero-eruptive xanthomas on the elbows.
6. Cerebrotendinous xanthomatosis (CTX) is due to a missing enzyme involved in bile acid synthesis (27 sterol hydroxylase CYP27) resulting in elevation in cholestanol. Cholestanol, a bile acid precursor, accumulates causing xanthomas and cataracts, and can lead to neurological problems including mental retardation. The treatment for CTX is bile acid replacement (UDCO), which shuts down bile acid synthesis and, therefore, cholestanol levels.

This 22-year-old woman has CTX. Although she had premature cataracts, the diagnosis was not made until the xanthoma was removed from her wrist for cosmetic reasons, which upon analysis revealed cholestanol confirming the diagnosis of CTX.

7. Familial phytosterolemia (beta-sitosterolemia) is a rare autosomal recessive condition due to mutation in ABCG5 or ABCG8, which actively removes non-cholesterol sterols after absorption through the NPC1L1 intestinal sterol transporter. These patients, therefore, hyperabsorb plant sterols causing tendon xanthoma, but plasma cholesterol concentrations may be normal or moderately elevated.
8. Deficiency of cholesterol 7-alpha hydroxylase (CYP7A1) causes severe hypercholesterolemia and gallstones. Deficiency of this enzyme markedly reduces bile acids in the bile and feces, the major route of cholesterol excretion, thereby increasing the pool of hepatic cholesterol downregulating LDL receptor activity.

In this 22-year-old woman, since both her parents have normal cholesterol levels, the differential diagnosis of her tendon xanthomas include ARH, familial phytosterolemia, and CTX. Familial hypercholesterolemia and familial defective Apo B are autosomal dominant conditions and, therefore, at least one parent would have to have hypercholesterolemia.

Items 8–10

True Answers: 8 (A, C, D); 9 (A, B, C, E); 10 (A, D)

A Relative Low Risk Woman with Elevated hs-CRP

In the JUPITER trial, patients on rosuvastatin had a lower cancer mortality ($P = .02$), but there was an increase in the development of type 2 diabetes. This increase in the rate of type 2 diabetes has also been noted in previous statin outcome trials. Another interesting benefit of rosuvastatin noted in the JUPITER trial was a significant decrease in venous thrombosis.

Statins lower hs-CRP in a dose-dependent manner. Statins with greater LDL-C-lowering efficacy lower hs-CRP more than do statins with lower efficacy. Drugs that lower hs-CRP in combination with statins include ezetimibe, fenofibrate, niacin, and colesevlam. Although they have cardioprotective benefits, omega-3 fatty acids do not lower hs-CRP.

NCEP ATP III guidelines emphasize the need to achieve specific goals for LDL-C in order to favorably alter clinical outcomes. However, statin therapy has the greatest absolute risk reduction in patients at the highest risk for CHD events. The JUPITER trial demonstrated that patients with inflammation, as measured by elevated hs-CRP and “normal LDL-C” (<130 mg/dL), achieved significant reduction in vascular events with potent LDL-C reduction (47%) with rosuvastatin 20 mg/day. Previous statin outcome studies have shown that the best clinical outcomes are achieved in very high risk patients if both LDL-C is <70 mg/dL and hs-CRP is <2.0 mg/L. The JUPITER investigators also prospectively evaluated whether the achieved dual targets of LDL-C and hs-CRP resulted in better clinical outcomes. As demonstrated in earlier trials, the JUPITER participants on rosuvastatin who achieved both LDL-C <70 mg/dL and hs-CRP <2.0 mg/L had fewer vascular events (Figure 2). This finding supports the conclusion that for people choosing to start statin therapy, reduction in both LDL-C and hs-CRP are indicators of the success of treatment.

The JUPITER trial, while supportive of dual targets of therapy, also provides compelling evidence that on-treatment LDL-C levels alone is a strong predictor of clinical benefit. Compared to placebo, participants allocated to rosuvastatin who did not achieve LDL-C <70 mg/dL, had no significant reduction in vascular events (placebo event rate 1.11%/year, participant allocated to rosuvastatin with LDL >70 mg/dL, event rate .91%/year, HR .89, 95% CI, .65–1.25, $P = .49$). On the other hand, patients allocated to rosuvastatin who had on-treatment hs-CRP >2.0 mg/L still had a significant benefit (event rate .7%/year), but not as much as those who achieved an hs-CRP <2.0 mg/L (event rate .42%/year) (Figure 2). In addition, participants who had $>50\%$ hs-CRP reduction had a lower event rate than those who achieved $<50\%$ hs-CRP reduction (.7%/year vs .17%/year). Finally, although the Apo B/A-1 ratio is the most powerful lipid predictor of vascular events, having a lower on-treatment hs-CRP <2.0 mg/L still predicted better clinical outcomes (Figure 3).

This woman would have qualified for the JUPITER trial since she was 60 years of age, with an LDL-C <130 mg/L, without type 2 diabetes or CHD, but with an hs-CRP ≥ 2.0 mg/L.

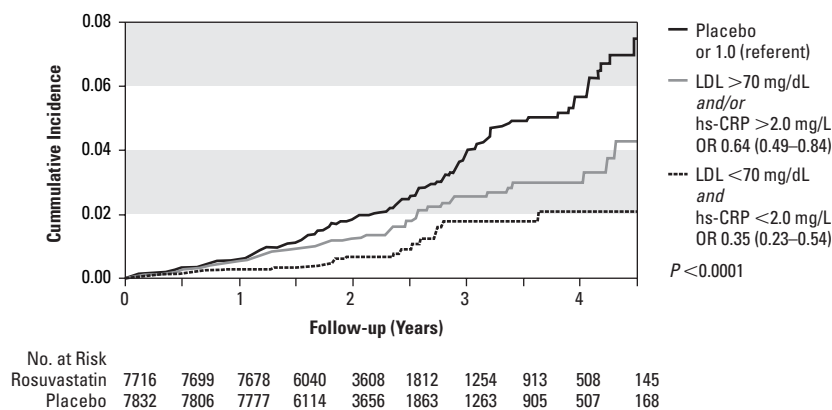


Figure 2. JUPITER Dual Target Analysis: LDL-C <70 mg/dL, hs-CRP <2.0 mg/L

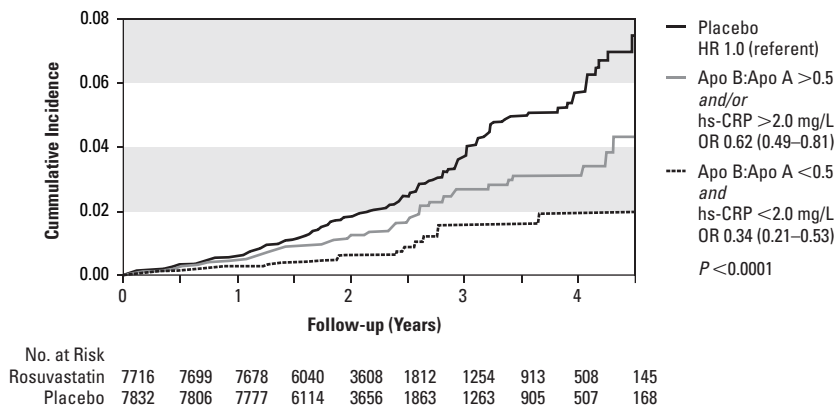


Figure 3. JUPITER Dual Target Analysis: Apo B: Apo A <0.5, hs-CRP <2.0 mg/L

Items 11–13

True Answers: 11 (A, B, C, D, E); 12 (A, B, E); 13 (A, B, C, D)

Statin Intolerance

Although statins are relatively well tolerated, approximately 5–10% of patients are intolerant. The most common cause of intolerance is statin-associated myalgias (SAMs) and muscle weakness. Patients with SAMs typically have normal or only slightly elevated CPK levels. This poorly understood side effect of statins may be due to a decrease in muscle ubiquinone or Co-enzyme Q10 levels. However, this theory has several limitations. Several studies in humans and animals have shown that statin treatment decreases serum Co-Q10 levels, but muscle ubiquinone levels are not consistently affected with data showing a slight decrease, no change, or an increase. Oral Co-Q10 supplementation studies in humans with statin intolerance have also been inconsistent with one small trial showing a benefit and another reporting no reduction in myalgias.

The risk factors for statin intolerance include hypothyroidism, old age, a family member with statin intolerance, and vitamin D deficiency. Recently, a gene variant has been identified (SLCO1B1) that has a high prevalence in patients with statin intolerance and myopathy. In the SEARCH trial, the SLCO1B1 variant was strongly associated with an increased risk of statin-induced myopathy (odds ratio 4.5). Another study (STRENGTH) verified this gene variant association with statin discontinuation due to statin muscle side effects.

The management of dyslipidemia in patients with statin intolerance is frequently challenging but some new data have provided some encouraging results. Since hypothyroidism appears to be strongly associated with SAMs and hypothyroidism alone causes muscle pain and weakness, aggressively managing the hypothyroidism will improve both LDL-C levels and muscle symptoms. The LDL receptor is a thyroid-regulated gene and, therefore, patients with slightly elevated TSH levels with high LDL-C levels, may have significant LDL-C reduction with thyroid replacement therapy. Recently, vitamin D deficiency has been linked to statin intolerance and vitamin D replacement improved statin feasibility in a majority of patients who had discontinued statin therapy due to myalgia.

In regards to therapeutic options in patients with statin intolerance, taking rosuvastatin twice a week improved LDL-C levels significantly and was well tolerated by this previously intolerant patient population. In 62 patients with dyslipidemia and a history of discontinuation of statin therapy due to myalgias, red yeast rice 1800 mg/day compared to placebo lowered LDL by approximately 20%. In addition, symptoms of myalgia were not different between those on red yeast rice or placebo.

Frequently, patients with statin intolerance need a combination of non-statin therapies to achieve significant LDL-C reduction. Ezetimibe alone lowers LDL-C by approximately 15–18%. Colesevelam can provide an additional 10–15% reduction, fenofibrate a 5–10% reduction, and niacin, depending on the dose, can lower LDL-C by up to 15–20% but usually requires 1500–2000 mg/day to achieve significant LDL-C reduction. Pioglitazone and prescription omega-3 fatty acids lower Apo B in patients with elevated triglycerides but do not lower LDL-C.

This patient would not qualify for reimbursement for LDL-apheresis according to Medicare guidelines. The Medicare guidelines are as follows:

1. Homozygous FH	LDL \geq 500 mg/dL
2. Heterozygous FH and failure of medical therapy	LDL \geq 300 mg/dL
3. Heterozygous FH with documented CHD and failure of medical therapy	LDL \geq 200 mg/dL

Items 14–15 True Answers: 14 (A, B, D); 15 (A, B, C, D, E)

Strong Family History of Premature CHD with Normal Lipid Profile

Genomic wide association studies (GWAS) have identified a number of gene variants associated with an increased risk of CHD. The most prominent of these gene variants is 9P21. Three studies published simultaneously demonstrated an association with a variant on chromosome 9P21 and CHD and type 2 diabetes. Approximately 21% of individuals of European descent are homozygous for this variant and the risk of having a myocardial infarction is 1.64-fold greater in them than in non-carriers. Other studies have estimated the risk to be approximately 1.3-fold greater. The mechanism by which this gene variant increases risk for CHD and type 2 diabetes is undergoing intense investigation.

About 60% of the American population are carriers of the KIF6 gene variant which has been shown to predict risk of CHD in both the CARE and WOSCOPS trials. In the Women's Health Study, KIF6 identified an increased risk of CHD in 25,283 initially healthy Caucasian American women age 45 and over. In the CARE and WOSCOPS trials, the patients with KIF6, while having a greater event rate than in the placebo group, also had a profound benefit with pravastatin therapy. This data suggests that KIF6 can assist in stratifying patients to more aggressive LDL-C reduction.

Lp(a) is a well recognized genetic factor associated with increased risk of CHD. PCSK9 deficiency causes low levels of LDL-C and is associated with lifelong protection for CHD. Elevated Apo A-II levels, similar to Apo A-I (but perhaps to a lesser degree), is associated with a decreased risk of CHD. Earlier data suggested that Apo A-II was not protective of CHD but most recent trials have confirmed that high levels of Apo A-II are linked to lower CHD rates.

With the marked increase in the prevalence of type 2 diabetes, there is increasing interest in biomarkers to enhance its prediction and thereby apply more aggressive preventive strategies. Hs-CRP, insulin, ferritin, adiponectin, and small dense LDL all predict the future development of type 2 diabetes. All of these factors are linked to insulin resistance, the precursor of clinical diabetes.

Items 16–20 True Answers: 16 (A, B, E); 17 (B, D, E); 18 (A, B, C, D, E); 19 (A, B, D); 20 (A, B, C, D, E)

A Patient with Recent Acute Coronary Syndrome and Metabolic Syndrome

Patients who have had acute coronary syndrome are at very high absolute risk for a recurrent event 2–3 years after the initial event. Targeting LDL-C treatment to below 70 mg/dL has achieved significant CVD benefits but a high residual risk continues in these patients, especially if other lipid parameters such as triglycerides (TGs) and HDL-C remain abnormal. Even though this 55-year-old Hispanic woman's LDL-C is <70 mg/dL, she continues to have a substantial increased risk of another cardiac event over the next 12 months. Identifiable residual risk factors include low HDL-C and HDL-P and elevated TGs, LDL-P, Apo B, hs-CRP, and Lp-PLA2. Although additional therapeutic interventions beyond statin therapy to modify these residual risk factors have not yet been proven, there is ample evidence that she remains at increased risk despite an LDL-C and non-HDL-C at goal (<70 and <100 mg/dL, respectively) according to the NCEP ATP III 2004 Update. However, according to the ADA/ACC Consensus Statement, she is not yet at her target of Apo B <80 mg/dL since she has cardiometabolic risk factors and CHD.

Increased Apo B and LDL-P levels have been shown to predict increased risk even if LDL-C is at target levels. In the Framingham Offspring Study, LDL-P was a more sensitive indication of low CVD risk than either LDL-C or non-HDL-C. The event-free survival rate was similar if the LDL-P were high but the LDL-C were low.

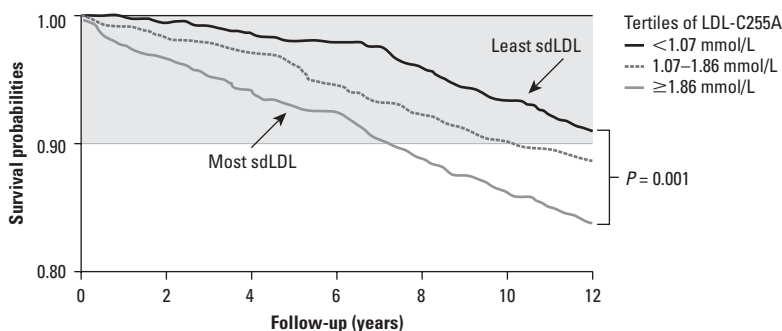


Figure 4. Increased Small, Dense, LDL Particles Associated with Reduced IHD Survival

IHD = ischemic heart disease

St-Pierre AC, et al: *Arterioscler Thromb Vasc Biol* 2005;25:553–9.

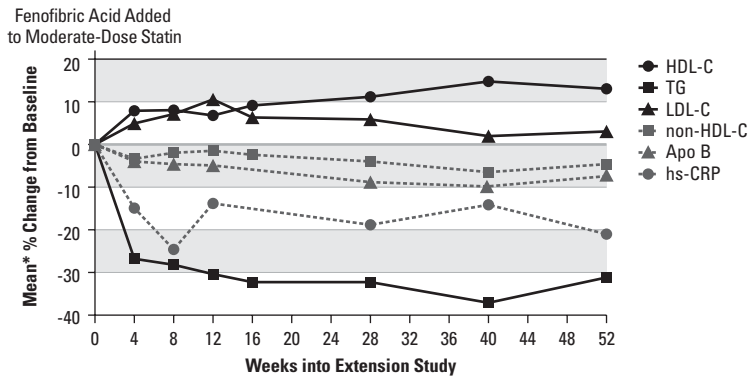
Lp-PLA2, an enzyme involved in atherogenesis, seems to preferentially bind to smaller LDL particles that are usually TG-enriched and carry electronegative charge. This may explain, at least in part, the mechanism by which more small LDL particles increase atherosclerotic progression. In general, non-HDL correlates better with Apo B than does LDL-C, especially if TGs are elevated. Usually, when TGs are elevated, LDL-P and Apo B are increased due to more predominant small LDL particles, but LDL-C is low or normal. However, in most studies after correcting for LDL-P, LDL size is no longer predictive of CHD events. A recent analysis for the IDEAL study showed that the Apo B/A-1 ratio is the most predictive of all the lipid parameters. A recent analysis of the EPIC Norfolk trial showed that both HDL particle (HDL-P) number and size were protective of CHD events.

In regards to add-on therapy to statin treatment in patients with hypertriglyceridemia, Table 1 summarizes the effect of different drugs on the various biomarkers associated with CVD risk.

Table 1.

	Omega-3 Fatty Acids	Fenofibrate/ Fenofibric Acid	Niacin
LDL-C	↑	—	↓
Non-HDL	↓	↓	↓
Triglycerides	↓↓	↓↓	↓
Apo B	↓	↓	↓↓
Apo A-1	—	↑	↑↑
LDL-P	—	—	↓
LDL size	↑	↑	↑
VLDL-P	↓	↓	↓
VLDL size	↓	↑↓	N/A
HDL-P	—	↑	↑
HDL-size	—	—	↑
Lp-PLA2	↓	N/A	N/A
hs-CRP	—	↓	N/A
Homocysteine	—	↑↑	↑
RLP-C	↓	↓	↓
Apo C-III	↓	↓	↓

Fenofibric acid, ezetimibe, and colesvelam lowers hs-CRP in combination with statins. Prescription omega-3 fatty acids does not appear to lower hs-CRP but does lower Lp-PLA2.



N (LDL-C)	364	354	334	336	321	316	306	292
Mean LDL-C (mg/dL)	92.9	95.0	96.3	100.0	96.1	95.4	92.5	92.5

Figure 5. Additional Efficacy During Extension Study

* Median % change is shown for TG and hs-CRP.

Bays HE, et al: *J Clin Lipidology* 2008;2:426–435.

Adding fenofibric acid to moderate dose statin (Figure 5) results in a significant additional decrease in TGs, non-HDL Apo B, and hs-CRP. LDL-C, but not Apo B, increases initially but over time returns to near baseline.

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CLM-SAP™

■ Edition 13

Challenging Cases in Dyslipidemia

Answer Sheet & Program Evaluation

■ Directions for Recording Answers

Make each mark heavy enough to completely obliterate the letter within the oval. Marks should fill the oval completely.

Erase clearly any answers you wish to change.

Make no stray marks on this answer sheet.

True-False Answer Sample

1
T F
Ⓐ ●
● Ⓑ
● Ⓒ
● Ⓓ
Ⓔ ●

Correct Marks



Incorrect Marks



■ CLM-SAP™ 13 Answer Sheet

1 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	5 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	9 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	13 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	17 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ
2 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	6 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	10 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	14 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	18 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ
3 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	7 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	11 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	15 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	19 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ
4 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	8 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	12 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	16 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ	20 T F Ⓐ Ⓐ Ⓑ Ⓑ Ⓒ Ⓒ Ⓓ Ⓓ Ⓔ Ⓔ

Carefully fold back and cut along the dotted line to remove.





Carefully fold back and cut along the dotted line to remove.

■ General Directions

In order to receive your CME/CE credit you must

1. Provide all of the following contact information including any address corrections.
2. Answer the Program Evaluation Questions below.
3. Complete, sign, date, and return this form to the National Lipid Association
by Fax: 904.998.0855 or by Mail: NLA, 6816 Southpoint Parkway, #1000, Jacksonville, FL 32216.

■ Personal Information

(Please type or print)

Name (Title)(First)	(M.I.)	(Last)	Degree
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Address

City	State	Zip
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Phone	eMail
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Specialty

■ CLM-SAP™ 13 Program Evaluation

Rating Scale: A = Outstanding B = Above Average C = Average D = Below Average E = Poor

1. Please rate the quality and effectiveness of the subject content of this CME/CE activity for Lipid Specialists. A B C D E

2. Please rate the relevancy/usefulness of the subject content of this CME/CE activity for your practice. A B C D E

3. After completing this activity, please rate your ability to:

Manage complex cases of dyslipidemia including a patient with severe hypertriglyceridemia; a patient with tendon xanthomas but no family history of heart disease; a low risk patient with elevated hs-CRP; a patient with statin intolerance; a patient with normal lipid profile but with a strong family history of premature CHD; and a patient with recent acute coronary syndrome and metabolic syndrome. A B C D E

Discuss the etiology of various types of complex dyslipidemia and the role of biomarkers. A B C D E

Recognize gene variations associated with complex dyslipidemia. A B C D E

4. Please rate the self-assessment and educational critique format of this CME/CE activity. A B C D E

5. Please rate this CME/CE activity regarding objectivity and neutrality of subject content A B C D E

6. As a result of participating in this activity, what will you be doing differently to improve the care of your patients?

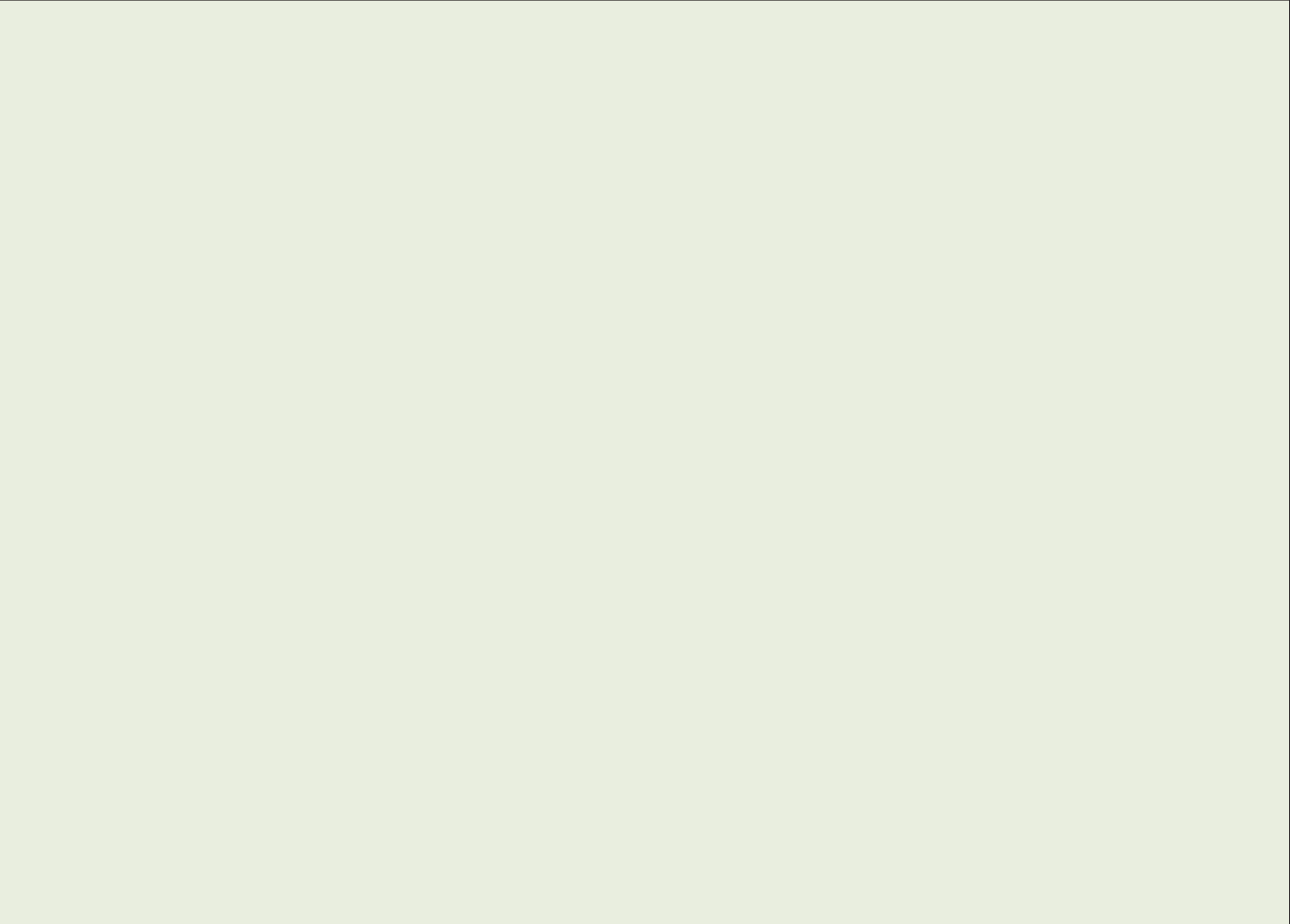
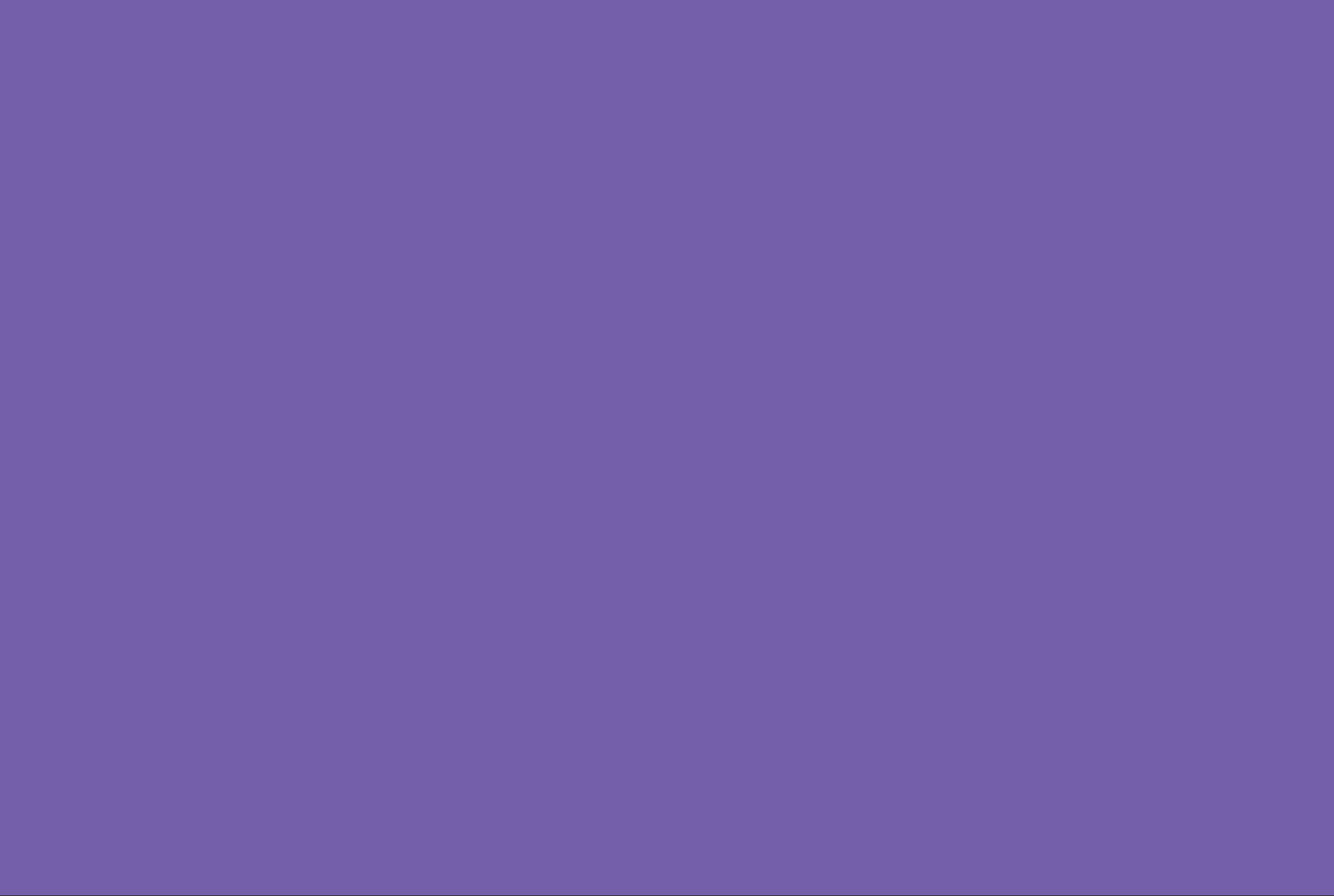
7. Overall, please rate this CME/CE activity. A B C D E

8. Are you interested in taking a certifying examination for Lipid Specialists?

A Yes B No C Undecided D Not Applicable

9. How many hours of CME/CE are you claiming? Claim only the number of hours, in 0.25 increments, which you actually participated. (maximum: 2.5) _____ hours

Signature Required	Date
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