

### ■ Items 35–39

For *each* numbered effect of atorvastatin on lipoprotein concentration or lipoprotein particles (35–39), select the one lettered patient phenotype (A, B, C, D, E) MOST likely associated with it. Each lettered patient phenotype may be selected *only once*.

- (A) Patients with LDL-C  $\geq 200$  mg/dL.
- (B) Patients with type II diabetes, LDL-C  $\geq 125$  mg/dL, and hypertriglyceridemia.
- (C) Healthy individuals with LDL-C  $< 150$  mg/dL and TG  $< 150$  mg/dL.
- (D) Patients described in options (A) and (B).
- (E) Patients described in options (A), (B) and (C).

- 35. Lowers LDL-C levels.
- 36. Does not change HDL-C or TG levels.
- 37. Decreases cholesterol content in all LDL subfractions.
- 38. Reduces cholesterol content to a similar degree in large-buoyant, intermediate dense, and small dense LDL subfractions.
- 39. Lowers triglycerides by 23.6%.

### ■ Items 40–41

You are referred a healthy 67-year-old menopausal woman (not on HRT), a non-smoker, whose father (a diabetic) died of a heart attack at the age of 55. She is currently on multiple antihypertensive medications (lisinopril, amlodipine, HCTZ) and requests a second opinion regarding initiating aspirin and lipid-lowering therapy. She has the following laboratory profile:

Total Cholesterol	226 mg/dL
Triglycerides	125 mg/dL
HDL-C	46 mg/dL
LDL-C	140 mg/dL
Glucose	110 mg/dL
Height	5'2"
Weight	151 lbs
Waist Circumference	36"
Blood Pressure	122/78 mm Hg

## ■ Items 53–57

A 45-year-old man with long-standing hypertension treated with antihypertensive agents and aspirin and a history of untreated dyslipidemia presented for a preventive cardiovascular evaluation and further therapy. He denied tobacco abuse or a family history of premature ASHD, although his grandfather did have a fatal myocardial infarction in his fifties. He was thin, exercised regularly, and ate a healthful diet. His past medical history was significant for vagally-mediated paroxysmal atrial fibrillation, mild mitral and aortic insufficiency, Thalassemia minor and occasional bronchitis. He consumed several nutritional supplements. Aside from his regurgitant murmurs, physical exam was unremarkable. Initial BP was 120/78 mm Hg. Initial CV laboratory data revealed the following:

Total Cholesterol	205 mg/dL
Triglycerides	44 mg/dL
HDL-C	52 mg/dL
LDL-C	144 mg/dL
LDL-P	1536 nmol/L
Small LDL-P	967 nmol/L
Homocysteine	8.03 mcmol/L
hs-CRP	0.23 mg/L
Lp(a)	6.5 mg/dL
Lp-PLA2	624 ng/ml

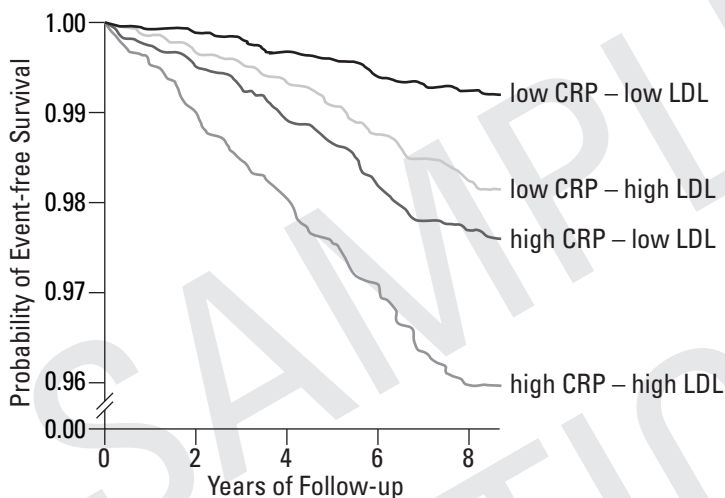
After reviewing his labs, a prolonged conversation ensued regarding his CV risks. Although his Framingham 10-year risk was calculated to be only 2%, the prognostic implications of his very high Lp-PLA2 result were considered. As a means of exploring his risk for coronary artery disease in greater detail, a 64 slice Coronary CT Angiogram (CCTA) was performed and it was found to be entirely normal (Figure 1). Vehemently opposed to the use of statins, he permitted only a very low dose statin to be prescribed for his elevated LDL and Lp-PLA2 levels. Follow up labs revealed the following:

Total Cholesterol	203 mg/dL
Triglycerides	43 mg/dL
HDL-C	53 mg/dL
LDL-C	142 mg/dL
LDL-P	1330 nmol/L
Small LDL-P	982 nmol/L
Homocysteine	6.77 mcmol/L
hs-CRP	10.01 mg/L
Lp(a)	<5.0 mg/dL
Lp-PLA2	293 ng/ml

**Item 43**

Answer E

None of the options listed is INCORRECT. With regard to subsequent vascular events, the PROVE IT-TIMI 22 trial indicated that the level of hs-CRP achieved after starting a statin was equal in importance to the achieved level of LDL-C (Figure 5). In addition, the REVERSAL trial indicated that atherosclerotic progression defined by IVUS was reduced more when levels of both hs-CRP and LDL-C were lowered. Measurement of hs-CRP is not required for this high risk patient and may not change the management strategy to reduce LDL-C to goal according to ATP III guidelines (specifically titrating the statin dose and potentially adding a second lipid-lowering agent to reach an LDL-C <70 mg/dL). Lifestyle changes that lower triglyceride levels and lower glucose values will also lower hs-CRP levels.

**Figure 5.****Bibliography**

1. Ridker P, et al: The Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 (PROVE IT–TIMI 22) Investigators. C-Reactive Protein Levels and Outcomes after Statin Therapy. *NEJM* 2005;352:20–28.
2. Nissen S, et al: The Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) Investigators. Statin Therapy, LDL Cholesterol, C-Reactive Protein, and Coronary Artery Disease. *NEJM* 2005;352:29–38.
3. Tsimikas S, et al: C-Reactive Protein and Other Emerging Blood Biomarkers to Optimize Risk Stratification of Vulnerable Patients *JACC* 2006;47:C19–C31.

**Item 44**

Answer C

All of the options are correct except C. While hs-CRP plays a role in the immune response, it is a circulating pentraxin that is produced in the liver, not a heme peroxidase secreted by phagocytes.

**Item 45**

Answer C

All of the therapies listed except for oral estrogen have been demonstrated in clinical trials to lower hs-CRP level. Oral estrogens have been noted to significantly increase hs-CRP levels, which may be due to their hepatic effects. Hs-CRP is produced in the liver and oral estrogens have a first pass hepatic effect that appears to stimulate hs-CRP production. This effect may also be due to the triglyceride-raising effects of oral estrogen because raloxifene, a selective estrogen receptor modulator that does not raise triglyceride levels, lowers hs-CRP levels. Statins, fenofibrate, weight loss, and rosiglitazone, which lower triglyceride levels, lower hs-CRP levels.

**Bibliography**

1. Koenig W, et al: C-Reactive Protein, a Sensitive Marker of Inflammation, Predicts Future Risk of Coronary Heart Disease in Initially Healthy Middle-Aged Men: Results From the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. *Circulation* 1999;99:23–242.