

■ Items 4–10

Niacin and fibrates are among the most efficacious drugs to raise HDL-C levels. For *each* numbered feature or mechanism of action for increasing HDL-C levels (4–10), select the *one* lettered drug(s) (A, B, C, D) associated with it. Each lettered drug(s) may be selected *once, more than once, or not at all*.

- (A) Niacin only.
- (B) Fibrates only.
- (C) Both niacin and fibrates.
- (D) Neither niacin nor fibrates.

4. Increase Apo A-II more than Apo A-I.
5. Increase LDL particle size.
6. Decrease LDL particle number.
7. Increase HDL-C with similar efficacy in patients with or without hypertriglyceridemia.
8. No dose adjustment necessary in patients with severe renal impairment.
9. Reduce uric acid level.
10. Demonstrated to reduce total mortality in clinical trials.

■ Items 11–15

For *each* numbered drug (11–15), select the *one* lettered proposed location (A, B, C, D, E) in Figure 1 for its major effect related to HDL metabolism. Each lettered proposed location may be selected *once, more than once, or not at all*.

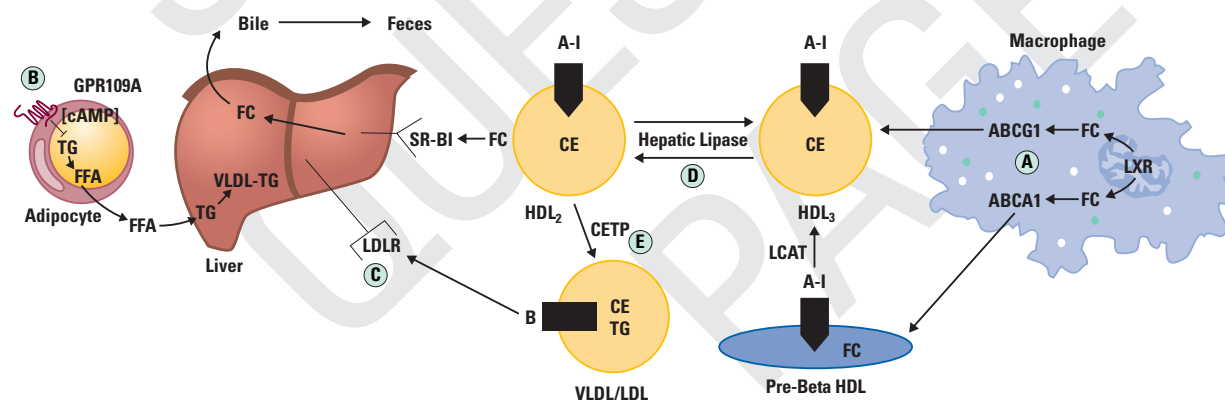


Figure 1.

11. Pioglitazone.
12. Torcetrapib.
13. Niacin.
14. Estrogen.
15. Rosuvastatin.

Her fasting laboratory values are as follows:

Total Cholesterol	212 mg/dL
HDL-C	43 mg/dL
LDL-C	139 mg/dL
Triglycerides	151 mg/dL
Non-HDL-C	169 mg/dL
Glucose	109 mg/dL
Lp(a)	41 mg/dL (nl <30)
Urine microalbumin/creatinine ratio	42 (nl <30)

36. Which *one* of the following criteria for the metabolic syndrome is this patient MISSING?
- (A) Elevated TG level.
 - (B) Increased waist circumference (using ATP III criteria).
 - (C) Elevated blood pressure.
 - (D) Elevated fasting glucose level (using ADA criteria for impaired fasting glucose).
 - (E) None of the above, she has all 5 criteria.
37. Which *one* of the following would NOT decrease her risk of developing type 2 diabetes mellitus?
- (A) Diet and exercise.
 - (B) Metformin.
 - (C) A thiazolidinedione.
 - (D) Estrogen replacement therapy.
 - (E) Hydrochlorothiazide.
38. Her risk of developing atherosclerosis is which *one* of the following?
- (A) Intermediate since she has an average LDL-C level, is a woman who is not yet clearly postmenopausal, and is well under 65-years-old.
 - (B) Moderately high because she is Hispanic and very likely to develop diabetes in the next couple of years.
 - (C) Moderately high because she is Hispanic and has the metabolic syndrome.
 - (D) Moderately high because she has a positive family history, low HDL-C, high TG, enlarged waist, microalbuminuria and likely has an excess of small, dense LDL particles.
 - (E) Low because her Framingham Risk Score is only 2% (13 total points).

Items 25–28

Answers 25 (B); 26 (E); 27 (E); 28 (A)

Under normal circumstances, HDL is an anti-inflammatory, anti-atherosclerotic particle, promoting reverse cholesterol transport (RCT) and efflux of inflammatory lipids from foam cells, improving endothelial function, limiting hemostasis, protecting LDL from oxidation, and decreasing vessel wall inflammation. This latter function is accomplished by inhibiting the expression of cytokine-induced cellular adhesion molecules on the surface of endothelial cells, the production of monocyte chemotactic protein-1 (MCP-1) by the vascular wall, and reduction in the amount of oxidized phospholipids.

In systemic inflammation and/or oxidative stress, HDL can lose its effectiveness as an anti-inflammatory particle and even assume some pathologic properties. This has been demonstrated by assays of HDL's effect on monocyte chemotaxis, phospholipid oxidation, cholesterol efflux, and endothelial adhesion molecules. Clinically, the development of “proinflammatory” HDL has been described in the postoperative period, in coronary disease patients, those with type 2 diabetes, rheumatologic conditions, and obstructive sleep apnea, among others conditions. Therapeutic lifestyle changes such as exercise, weight loss, and emphasizing dietary polyunsaturated fat (in lieu of saturated sources) have been associated with improved HDL anti-inflammatory function. At this time, the only available pharmacologic agents with proven qualitative impact on HDL anti-inflammatory function are statins.

Bibliography

1. Ansell BJ, et al: High Density Lipoprotein Function: Recent Advances. *JACC* 2005;46(10):1792–1798.
2. Ansell BJ, et al: The paradox of dysfunctional high density lipoprotein. *Curr Opin Lipidol* 2007;18(4):427–34.

Item 29

Answer D

AIM-HIGH is a five-year lipid treatment trial that compares how simvastatin taken alone or with extended-release niacin may reduce the risk of cardiovascular disease in subjects with established atherosclerotic disease and low HDL-C levels.

Major inclusion criteria of AIM-HIGH include:

1. Age at least 45 years old.
2. Evidence of atherosclerosis manifested by:
 - History of myocardial infarction.
 - History of previous stroke.
 - History of hospitalization for acute coronary syndrome.
 - History of occlusive vascular disease.
3. Lipid levels:
 - LDL-C <180 mg/dL (4.65 μ mol/L in Canada).
 - TG >100 mg/dL but <400 mg/dL (between 1.70–4.52 μ mol/L in Canada).
 - HDL-C <40 mg/dL (1.03 μ mol/L in Canada) (men) or HDL-C <50 mg/dL (1.29 μ mol/L) (women).

Exclusion criteria include:

- Coronary bypass surgery within the past year or PTCA within the past month.
- Recent history of gout.
- Uncontrolled diabetes.

Bibliography

1. www.aimhigh-heart.com, accessed November 25, 2007.